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CLINICAL SIGNIFICANCE OF STAPHYLOCOCCI

WITH NATURAL OR ACQUIRED RESISTANCE TO THE SULFONAMIDES AND TO PENICILLIN

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A problem of considerable importance in the chemotherapy of infectious diseases has been the development and dissemination of sulfonamide resistant strains of bacteria. Strains of micro-organisms within the different species known to be highly susceptible to the antibacterial action of the sulfonamides have acquired the characteristic of multiplying in the presence of high concentrations of the drugs. This acquired resistance appears to be a permanent property of these strains, and the resistant organisms are just as invasive as their sulfonamide sensitive progenitors. The mechanism whereby species of bacteria become relatively resistant to the sulfonamides is not completely understood, but it is related to the exposure of sensitive organisms to sublethal concentrations of the sulfonamides. Clinicians are rapidly becoming aware of the increasing incidence of gonorrhea in patients in whom the disease cannot be eradicated with intensive sulfonamide therapy. To a lesser extent this also applies to other bacterial infections such as those due to the pneumococcus and the hemolytic streptococcus. Fortunately, some strains of bacteria which develop resistance to the action of the sulfonamides may be highly susceptible to penicillin.

Our purpose in this report is to review briefly a group of investigations which have been carried out in this clinic with reference to the resistance of staphylococci to the action of the sulfonamides. More recently, further observations have been made pertaining to the problem of natural and acquired resistance of staphylococci to penicillin. These biologic phenomena may have a direct bearing on the success or failure of chemotherapy in staphylococcic sepsis. With more and more penicillin being made available for civilian use, increasing interest is being manifested in strains of staphylococci which are naturally resistant to the action of penicillin or acquire a resistance to the drug. An attempt has been made to correlate clinical results with strain resistance to the sulfonamides and, especially, to penicillin.

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SULFONAMIDE RESISTANT STAPHYLOCOCCI

It is generally agreed that penicillin is superior to any of the available sulfonamides in the therapy of staphylococcic infections. Nevertheless, the problem of penicillin resistant strains of staphylococci may be best approached by reviewing some of the investigations which have been made relative to the antistaphylococcic action of the sulfonamides. In determining the susceptibility of staphylococci to the sulfonamides, a standard in vitro test has been employed with a chemically defined medium; the preparation of the medium and the method of testing have been described elsewhere.[1] From these observations the following have been concluded: 1. Sulfathiazole inhibited the growth of coagulase positive strains of staphylococci more consistently and completely than sulfanilamide, sulfapyradine, sulfadiazine and, more recently, sulfamerazine. The action of sulfathiazole, of all the foregoing sulfonamides, was the least inhibited by para-aminobenzoic acid.[2] 2. Strains of pathogenic staphylococci may develop resistance in vivo to the antistaphylococcic action of sulfathiazole following the administration of the compound to patients with staphylococcic infections. Subsequently this observation was correlated with the clinical results of sulfonamide therapy.[3] During the past three years, sulfonamide resistant strains have been encountered with increasing frequency, particularly in patients having infections of the urinary tract. This was attributed to the widespread and often continuous use of the sulfonamides in the treatment of patients with this type of staphylococcic infection. In several instances there was a close correlation between the in vitro resistance of a strain to sulfathiazole and the success or failure of sulfonamide therapy. 3. In studying the mechanism whereby staphylococci became resistant to the sulfonamides, the observation of Landy and his associates[4] was confirmed in that resistant strains elaborated an inhibitory substance consistent with para-aminobenzoic acid or closely related to it.[5] This has been further confirmed by Housewright and Koser.[6]

1. Spink, W. W., and Vivino, J. J.: Sulfonamide Resistant Staphylococci: Correlation of In Vitro Sulfonamide Resistance with Sulfonamide Therapy, J. Clin. Investigation **23**: 267 (March) 1944.

2. Spink, W. W., and Jermsta, J.: Effect of Sulfonamide Compounds on Growth of Staphylococci in Presence and Absence of *p*-Aminobenzoic Acid, Proc. Soc. Exper. Biol. & Med. **47**: 395 (June) 1941.

3. Vivino, J. J., and Spink, W. W.: Sulfonamide Resistant Strains of Staphylococci: Clinical Significance, Proc. Soc. Exper. Biol. & Med. **50**: 336 (June) 1942. Spink and Vivino.[1]

4. Landy, M.; Larkum, N. W.; Oswald, E. J., and Streightoff, F.: Increased Synthesis of *p*-Aminobenzoic Acid Associated with the Development of Sulfonamide Resistance in Staphylococcus Aureus, Science **97**: 265 (March 19) 1943.

5. Spink, W. W.; Wright, L. D.; Vivino, J. J., and Skeggs, H. R.: Para-Aminobenzoic Acid Production by Staphylococci, J. Exper. Med. **79**: 331 (April) 1944.

6. Housewright, R. D., and Koser, S. A.: A Study of the Para-Aminobenzoic Acid Requirement of Clostridium Acetobutylicum: Application to Assay Procedure, J. Infect. Dis. **75**: 113 (Sept.-Oct.) 1944.

4. Strains of pathogenic staphylococci which had acquired a high degree of resistance to sulfathiazole by either in vitro or in vivo methods remained just as invasive as the sensitive parent strains. This acquired sulfonamide resistance is apparently a permanent characteristic of the staphylococci, since in a period of two years following many subcultures the strains have not diminished in resistance.

PENICILLIN RESISTANT STAPHYLOCOCCI

In view of the foregoing experience with the sulfonamides, it appeared highly desirable to carry out a similar group of investigations with penicillin and a large number of coagulase positive strains of staphylococci isolated from patients. The information which we wished to obtain was Do strains of pathogenic staphylococci vary in their susceptibility to the in vitro action of penicillin? Is strain variation reflected in the results of therapy? Does the staphylococcus acquire a resistance to penicillin following in vitro and in vivo exposure of the organisms to the drug? If resistance may be acquired, are the resistant strains just as invasive as the sensitive parent strains, and is the resistance a permanently acquired characteristic? And, finally, may clinical failures with penicillin be correlated with the in vivo development of penicillin resistance?

In the first group of studies, 68 strains of coagulase positive staphylococci were isolated from patients none of whom had received penicillin. The in vitro sensitivity of each of these strains to penicillin was compared with their susceptibility to sodium sulfathiazole.[7] Included in these strains were 25 strains which were resistant to sulfathiazole. It was observed that 8 of the 68 strains, or 12 per cent, were relatively resistant to penicillin, requiring 0.4 to 0.8 unit of penicillin per cubic centimeter of culture medium before growth was inhibited. Many of the sulfonamide resistant strains proved to be quite susceptible to penicillin. In other words, there was no correlation between sulfonamide resistance and susceptibility of the organisms to the action of penicillin. Kirby,[8] who has also recorded the isolation of naturally resistant strains of staphylococci from patients, was able to extract a potent inactivator of penicillin from such strains but not from strains of staphylococci sensitive to penicillin. We have confirmed this observation of Kirby.

The preceding observations indicated that the mode of action of penicillin on staphylococci differed from that of the sulfonamides, and this is now generally accepted. Penicillin appears to inhibit the growth of sensitive organisms by interfering with the dividing bacterial cell or one that is about to divide.[9] The action of penicillin is assumed to be bacteriostatic and, under some conditions, bactericidal. Rantz and Kirby[10] reported that penicillin was bacteriolytic for staphylococci. Since the sulfonamides differ from penicillin in their mechanism of inhibiting growth of the staphylococci, it might be assumed that the combined use of a sulfonamide and penicillin would be desirable in the treatment of some patients with staphylococcic infections. However, experimental data as a basis for such a procedure are conflicting. Some investigators[11] have shown by in vitro methods that the bacteriostatic action for penicillin is greater in the presence of sulfonamide than with penicillin alone, but this is not in agreement with the reports of others.[12]

The studies were continued by adapting four coagulase positive strains of staphylococcus to grow in the presence of increasing concentrations of penicillin.[13] In this manner two strains developed a high degree of resistance to the antistaphylococcic action of penicillin. One strain, which required 0.04 unit of penicillin per cubic centimeter to inhibit growth before adaptation, required 80 units after a period of several weeks' exposure to penicillin. A second strain, originally inhibited by 0.06 unit, necessitated 120 units for complete inhibition of growth after adaptation. Both of these strains remained quite sensitive to sodium sulfathiazole. Two other strains, decidedly resistant to sodium sulfathiazole but sensitive to penicillin, were adapted to grow in penicillin, with the result that the strains manifested a resistance to both sodium sulfathiazole and to penicillin. This confirmed the results of others[14] that staphylococci may develop in vitro resistance to penicillin and offered further evidence that the mechanism of acquired sulfonamide resistance differed from penicillin resistance. Schnitzer and his group[15] have stated that there are three types of penicillin resistant staphylococci. The first type includes strains with natural resistance, the second embraces the strains which acquire resistance, and the third involves small colony variants (G forms) of a strain of Staphylococcus albus which exhibited a nonspecific form of penicillin resistance. Demerec[16] has presented evidence that the development of in vitro resistance of staphylococci to penicillin does not result from the action of penicillin on the organisms but originates through a selective process whereby nonresistant individuals are eliminated by the drug, and, through mutation, the more resistant cocci multiply.

We have also observed that organisms which developed resistance to penicillin by in vitro methods were killed in considerable numbers by human whole blood, whereas the sensitive parent strains and also sulfonamide resistant strains resisted this bactericidal action of blood. It is of interest that, although the penicillin resistant strains retained their ability to coagulate human plasma, they lacked the usual degree of resistance to the bactericidal action of blood exhibited uniformly by coagulase positive strains of staphylococci.[17] It has also been previously shown in this laboratory that the less invasive coagulase negative

7. Spink, W. W.; Ferris, V., and Vivino, J. J.: Comparative In Vitro Resistance of Staphylococci to Penicillin and to Sodium Sulfathiazole, Proc. Soc. Exper. Biol. & Med. **55**: 207 (March) 1944.

8. Kirby, W. M. M.: Extraction of a Highly Potent Penicillin Inactivator from Penicillin Resistant Staphylococci, Science **99**: 452 (June 2) 1944.

9. Gardner, A. D.: Morphological Effects of Penicillin on Bacteria, Nature, London **146**: 837 (Dec. 28) 1940. Hobby, G. L.; Meyer, K., and Chaffee, E.: Observations on the Mechanism of Action of Penicillin, Proc. Soc. Exper. Biol. & Med. **50**: 281 (June) 1942. Bigger, J. W.: Treatment of Staphylococcal Infections with Penicillin by Intermittent Sterilization, Lancet **2**: 497 (Oct. 14) 1944.

10. Rantz, L. A., and Kirby, W. M. M.: The Action of Penicillin on the Staphylococcus in Vitro, J. Immunol. **48**: 335 (June) 1944.

11. Ungar, J.: Synergistic Effect of Para-Aminobenzoic Acid and Sulfapyridine on Penicillin, Nature, London **152**: 245 (Aug. 28) 1943. Bigger, J. W.: Synergic Action of Penicillin and Sulfonamides, Lancet **2**: 142 (July 29) 1944. Kirby, W. M. M.: Bacteriostatic Action of Sulfonamide-Penicillin and Urea-Penicillin Mixtures in Vitro, Proc. Soc. Exper. Biol. & Med. **57**: 149 (Oct.) 1944.

12. Hobby, G. L., and Dawson, M. H.: Relationship of Penicillin to Sulfonamide Action, Proc. Soc. Exper. Biol. & Med. **56**: 184 (June) 1944. Garrod, L. P.: Action of Penicillin, Lancet **2**: 673 (Nov. 18) 1944.

13. Spink, W. W.; Ferris, V., and Vivino, J. J.: Antibacterial Effect of Whole Blood on Strains of Staphylococci Sensitive and Resistant to Penicillin, Proc. Soc. Exper. Biol. & Med. **55**: 210 (March) 1944.

14. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Observations on Penicillin, Lancet **2**: 117 (Aug. 16) 1941. Rammelkamp, C. H., and Maxon, T.: Resistance of Staphylococcus Aureus to the Action of Penicillin, Proc. Soc. Exper. Biol. & Med. **51**: 386 (Dec.) 1942. McKee, C. M., and Houck, C. L.: Induced Resistance to Penicillin of Cultures of Staphylococci, Pneumococci and Streptococci, ibid. **53**: 33 (May) 1943.

15. Schnitzer, R. J.; Camagni, L. J., and Buck, M.: Resistance of Small Colony Variants (G Forms) of a Staphylococcus Toward the Bacteriostatic Activity of Penicillin, Proc. Soc. Exper. Biol. & Med. **53**: 75 (May) 1943.

16. Demerec, M.: Production of Staphylococcus Strains Resistant to Various Concentrations of Penicillin, Proc. Nat. Acad. Sc. **31**: 16 (Jan.) 1945.

17. Spink, W. W., and Vivino, J. J.: The Coagulase Test for Staphylococci and Its Correlation with the Resistance of the Organisms to the Bactericidal Action of Human Blood, J. Clin. Investigation **21**: 353 (May) 1942.

strains of staphylococci were, with rare exceptions, killed in large numbers by human whole blood. This suggested, at least, that the metabolic activity of the penicillin resistant strains had undergone a change and the organisms had become less virulent. But this has little or no clinical significance, since organisms which have become resistant to penicillin in the human body are as resistant to the bactericidal action of human blood as the penicillin sensitive parent strains.

Several strains of staphylococci which had developed a high degree of resistance to the sulfonamides by in vitro adaptation have retained this resistance without diminution for almost three years. In other words, the acquisition of resistance to the sulfonamides by staphylococci appears to be a permanently acquired characteristic. It appeared at first that this also applied to staphylococci with acquired penicillin resistance, because the first few subcultures revealed that the organisms retained this insensitivity. However, further subcultures of four strains showed that the organisms had lost this acquired resistance. At the same time, these strains reverted to resisting the killing power of human whole blood to the same degree as the penicillin sensitive parent strains. Strains made resistant to both sulfathiazole and penicillin showed no decrease in sulfonamide resistance, even though the acquired pencillin resistance was lost. Further investigations in this laboratory have revealed that strains of staphylococci which have become resistant to penicillin in the human body following the administration of penicillin to patients develop a resistance which is probably permanent, and this in vivo strain resistance is associated with the production by the organisms of a potent inhibitor of penicillin activity.

The foregoing data on the sulfonamides and penicillin may be summarized as follows: Coagulase positive strains of staphylococci may be readily adapted to grow in the presence of high concentrations of the sulfonamides by laboratory methods as well as by exposing the organisms to the drugs in the human body. These sulfonamide resistant strains appear to be just as invasive as the parent strains, and sulfonamide resistance is apparently a permanently acquired characteristic. The development of sulfonamide resistance is quite likely related to the elaboration of a sulfonamide inhibitor which is para-aminobenzoic acid or closely related to it. Recently Sevag and Green [18] have taken exception to this concept and have concluded "that the development of resistance to sulfonamides is associated with the development of a sulfonamide resistant type of glucose metabolism." Confirmation of their work is highly desired and necessary. Strains of coagulase positive staphylococci may be less readily adapted to resist the action of penicillin than that of the sulfonamides. Strains highly resistant to the sulfonamides may also develop a considerable degree of resistance to penicillin. Strains of staphylococci naturally resistant to penicillin produce an inhibitor of penicillin activity. Such an inhibitor has not been obtained from sensitive strains. The development of resistance of staphylococci to penicillin by in vitro methods is only a temporary biologic phenomenon. Such strains rapidly lose this property in the absence of penicillin. An inhibitor of penicillin is not obtained from strains made resistant by in vitro methods. On the other hand, strains of staphylococci which have become resistant in vivo as a result of therapy with penicillin retain this resistance as a permanent characteristic, and these resistant strains produce a potent inhibitor of penicillin activity.

18. Sevag, M. G., and Green, M. N.: The Mechanism of Resistance to Sulfonamides: II. Absence of Correlation Between Resistance and the Formation of Arylamine by Staphylococcus Aureus; Noninterference with the Utilization of Glucose as a Critical Factor in the Development of Resistance to Sulfonamides, J. Bact. **48**: 623 (Dec.) 1944.

CLINICAL CONSIDERATIONS

The crystallization of these and similar laboratory investigations with reference to an interpretation of clinical results is beset with many difficulties. However, an organism manifesting a high degree of susceptibility to penicillin in the test tube is usually sensitive to equivalent amounts of penicillin in the human body. In fact, a higher degree of bacterial destruction may be anticipated in the body, since, in addition to penicillin, there is the added factor of a natural or acquired immune mechanism. This correlation does not apply so uniformly to the sulfonamides because of the presence of factors present in the tissues and body fluids which inhibit the action of the sulfonamides. When the newer sulfonamide derivatives were introduced into medicine, more potent antistaphylococcic agents became available. And yet such compounds as sulfathiazole and sulfadiazine proved to be less satisfactory than anticipated. Among other deficiencies it appeared that strains of staphylococci developed an increased resistance to the sulfonamides and that these strains were being disseminated. Since penicillin is a superior agent in the treatment of practically all infections due to staphylococci, at the present time in this clinic sulfadiazine and sulfathiazole are being reserved principally for the treatment of some urinary tract infections in which sensitivity tests reveal that the growth of the offending strain of staphylococcus is inhibited by low concentrations of these compounds. Therapeutic failures have invariably attended the treatment of patients with sulfonamides where in vitro tests showed the staphylococci to be highly resistant to the sulfonamides. Sulfathiazole is also being employed simultaneously with penicillin for a selected group of patients with other types of staphylococcic infections.

Little data have been recorded in the literature pertaining to the clinical results with penicillin where staphylococci have manifested a natural or acquired in vitro resistance to penicillin. Bloomfield and his associates,[19] in a timely review of therapeutic failures encountered in their clinic, concluded that the development of organisms resistant to penicillin is probably of little importance but that there is very likely a correlation between initial in vitro strain sensitivity and the response to penicillin. Keyes,[20] in a discussion of the use of penicillin in ophthalmology, stated that the early treatment with inadequate concentrations of penicillin may result in the development of insensitive organisms. Under these circumstances intensive treatment with penicillin or the combined or alternate use of sulfonamides should be tried. In the treatment of chronic staphylococcic infections he suggests a preliminary in vitro test of sensitivity of the organisms. Anderson and his associates [21] have reported on the use of penicillin in the treatment of 40 cases of chronic osteomyelitis. In 5 cases there was no improvement, and in 4 of these failure to improve was considered as being due to the fact that the organisms became resistant to penicillin. In 19 of the patients the sensitivity of the organisms cultured from local lesions was tested before therapy, and then one or more weeks after therapy

19. Bloomfield, A. L.; Kirby, W. M. M., and Armstrong, C. D.: A Study of "Penicillin Failures," J. A. M. A. **126**: 685 (Nov. 11) 1944.
20. Keyes, J. E. L.: Penicillin in Ophthalmology, J. A. M. A. **126**: 610 (Nov. 4) 1944.
21. Anderson, D. G.; Howard, L. G., and Rammelkamp, C. H.: Penicillin in the Treatment of Chronic Osteomyelitis: Report of 40 Cases, Arch. Surg. **49**: 245 (Oct.) 1944.

organisms which persisted in the lesions were tested again. Five strains revealed an increase in resistance, and, in 2 of the cases, cultures made a year after the completion of therapy with penicillin showed the organisms to be still resistant to penicillin. There was no correlation between the development of resistance and the dose of penicillin administered to the patients.

At the University of Minnesota Hospitals, 69 patients with staphylococcic infections have received penicillin. Thirty-one of the patients had a bacteremia. A report summarizing the results of therapy will be presented elsewhere. Whenever possible, the in vitro sensitivity of the staphylococcus to penicillin was determined before and after therapy. Among the cases of bacteremia there were nine deaths, and there was no convincing evidence that a fatal issue was associated with the development of penicillin resistant strains of staphylococci. Of the 38 patients without bacteremia, in only 2 instances was there evidence that staphylococci with acquired resistance may have prevented complete eradication of the infection; but the evidence was not conclusive. One of these patients had chronic osteomyelitis with a draining sinus, and the second had a draining sinus which followed a nephrectomy for pyelonephritis and a perirenal abscess. In analyzing all of the cases treated there was no certainty that naturally resistant strains of organisms were the cause of a therapeutic failure. Failure to eradicate infections was due to two main causes: First, the use of inadequate amounts of penicillin, owing in several instances to a scarcity of the material. In the treatment of infections caused by naturally resistant organisms, this factor of inadequate dosage may be quite important. But the degree of natural resistance is relative. The sensitivity test as used in this laboratory has failed to reveal a strain of staphylococcus not previously exposed to penicillin that was not inhibited by 1 unit of penicillin per cubic centimeter of medium, and well over 100 strains have been tested. While this concentration of penicillin in the plasma is not readily attained in patients by the administration of even large doses of penicillin, we have observed that doses of penicillin calculated to give a concentration of 0.2 to 0.3 unit per cubic centimeter of plasma have rapidly sterilized the blood when the in vitro test showed that 0.8 to 1 unit of penicillin was necessary to inhibit growth. This discrepancy may possibly be explained by the fact that the additive effect of penicillin aided the immune factors of the host in overcoming infections. In the treatment of staphylococcic infections, and particularly bacteremia, it is desirable in many instances to maintain blood concentrations of 0.2 to 0.3 unit of penicillin per cubic centimeter, especially when the sensitivity of the organisms is not known. Rantz and Kirby [22] have found that during the continuous intravenous administration of penicillin 2,500 units of penicillin per hour resulted in a concentration of 0.05 unit per cubic centimeter in the plasma; 5,000 units per hour, 0.10 unit; 10,000 units per hour, 0.2 unit; and 20,000 units per hour, 0.4 unit. We have observed that the growth of the majority of strains of coagulase positive staphylococci is inhibited in the test tube by 0.2 unit of penicillin or less. In the treatment of severe staphylococcic bacteremia we have had reasonably satisfactory results during the initial stages of therapy when we have used 200,000 to 300,000 units over a period of twenty-four hours. This means that the plasma concentration of penicillin approximated 0.2 unit per cubic centimeter during this period. On the other hand, in many instances the blood stream has been rapidly cleared of organisms when one-half this dose has been used.

The second group of causes for failures in therapy with penicillin has been the persistence of foci such as a staphylococcic endocarditis and thrombophlebitis involving the larger veins of the lower extremities; and the presence of relatively avascular infected tissues which interfere with direct contact of penicillin with the bacteria such as occurs in bone infections and in some types of infections of soft tissues. Under these circumstances surgical eradication of the foci, whenever possible, is a necessary procedure.

COMMENT

Since penicillin is now the most potent chemotherapeutic agent available for staphylococcic infections, there are only limited indications for the use of the sulfonamides. Until more information is available, in this clinic selected cases with urinary tract infections due to staphylococci are being treated with sulfathiazole or sulfadiazine. Most of the cases are chosen on the basis that the organisms manifest in vitro sensitivity to the sulfonamides. Patients having infections due to organisms which are sulfonamide resistant do not usually respond to sulfonamide therapy. While it would appear desirable to employ sulfathiazole or sulfadiazine along with penicillin in the treatment of a severe staphylococcic infection when the organisms are naturally resistant to penicillin but susceptible to the sulfonamide, there is a paucity of clinical information along these lines. Lockwood and his group [23] apparently successfully combined sulfonamide therapy with penicillin in a case of severe staphylococcic bacteremia. During the past two years we have been determining the in vitro sensitivity of staphylococci isolated from patients with staphylococcic bacteremia to both sodium sulfathiazole and to penicillin in an attempt to resolve this problem. Thus far it would appear that such a combination is probably unnecessary in the vast majority of patients, provided adequate amounts of penicillin are used.

From our observations over a period of two years, and from those of others, it is becoming more manifest that the development of penicillin resistant staphylococci during therapy is not a major problem. However, such a biologic phenomenon may influence the outcome of treatment in an occasional patient. The development of resistance is very likely dependent on the exposure of the cocci to sublethal concentrations of penicillin. Therefore the aim of therapy should be to eradicate the largest number of organisms in the shortest period of time. This implies the use of adequate doses of penicillin, particularly in the treatment of severe infections, and the eradication of any relatively avascular foci by surgical means. Since occasional strains of staphylococci appear to develop a permanent resistance to penicillin, the dissemination of these strains may be associated with therapeutic failures. Thus far this does not appear to have much clinical significance.

SUMMARY

1. Sulfonamide resistant strains of coagulase positive staphylococci are being recovered with increasing frequency from patients. This resistance appears to be a permanently acquired characteristic, and the development of resistance is not associated with a diminution in virulence.

22. Rantz, L. A., and Kirby, W. M. M.: The Absorption and Excretion of Penicillin Following Continuous Intravenous and Subcutaneous Administration, J. Clin. Investigation **23**: 789 (Sept.) 1944.

23. Lockwood, J. S.; White, W. L., and Murphy, F. D.: The Use of Penicillin in Surgical Infections, Ann. Surg. **120**: 311 (Sept.) 1944.

2. Coagulase positive strains of staphylococci are occasionally encountered which possess a natural resistance to penicillin. While this biologic phenomenon may be conducive to therapeutic failures with penicillin, the resistance is relative and may be overcome with adequate doses of penicillin. For this reason it is recommended that adults having severe staphylococcic infections should receive a minimum of 200,000 units of penicillin each twenty-four hours during the initial stages of therapy.

3. Coagulase positive strains of staphylococci may acquire in vitro and in vivo resistance to penicillin. The resistance to penicillin which has been developed by in vitro methods is only a temporary characteristic of the organisms. Resistance acquired in vivo as a result of therapy with penicillin appears to be a more permanently acquired property of the bacteria. Thus far the development of such resistance appears to be a minor cause of failures with penicillin.

4. Since some strains of coagulase positive staphylococci may show a resistance to penicillin but pronounced sensitivity to sulfathiazole or to sulfadiazine, it would appear desirable to utilize a combination of penicillin and sulfonamide therapy. However, more clinical evidence is required before ascertaining the merit of such a procedure.

TRAUMATIC INJURIES OF THE RECTUM

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At a previous meeting of this section I[1] discussed the operative injury of the anal sphincter. The present topic is a sort of sequel and is also apropos to current emphasis on traumatic surgery. The intraperitoneal complications of rectal injuries and concomitant damage to neighboring organs such as the bladder have been primarily stressed heretofore and rather fully reported (as their seriousness deserves) and hence will not concern us here.

On the other hand there is little to be found concerning the perineal issues alone and particularly their own essential significance in relation to devastating and even fatal sequelae. I do not have in mind the occasional unfortuitous complications of surgery in general but consequences inexorably determined by the surgeon's deliberate plan of operation and under his responsible control. These considerations not only pertain to traumatic injuries but comprise basic proctologic principles which even in their more obvious connections with commoner rectal pathologic conditions are too frequently disregarded by the surgeon. Hence my present remarks are of actually much wider import than the restricted subject implies.

The perineal complications of rectal injuries spring primarily from the innate and persistent tendency of such wounds to be fistulous in character. Now no one has reduced to anything approaching precise terms the behavior of tissues in explanation of fistula formation; in a vague and uncritical assumption that we understand this, a degree of familiarity with conditions predicating fistula formation and the bare sequence of events have been confused with actual knowledge of cause and effect. Even the conditions and sequences themselves, although well established, fail of ample cognizance.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Blaisdell, Paul C.: Operative Injury to the Anal Sphincter, J. A. M. A. **112**: 614 (Feb. 18) 1939.

Let us first picture a penetrating wound from the perianal skin into the rectum (fig. 1). Certainly all would recognize this without equivocation as a fistulous wound even though it is difficult to explain precisely why; wounds in general are wont to heal if their fresh edges are in such close apposition; it is infected—yes, but even infected wounds do heal, and, conversely, a fistula inaugurated in measure by fecal contamination may fail to heal even when freed from this influence; as far as that is concerned, sinuses originate (and persist) entirely apart from any fecal soiling whatever. For the moment, however, the point is to visualize the indisputable basic concept of a fistulous wound for comparison with a lacerated wound, which is the most common pattern of traumatic rectal injury (fig. 1). Unfortunately, the key to its proclivities and management is too frequently sought, perhaps unwittingly, in analogies with lacerations elsewhere in the body, both more frequent and familiar, rather than in the unrecognized imagery of the penetrating wound. To come at once to the point, such traumatic lacerated wounds of the rectum should be thought of in terms of penetrating wounds which lack only variable amounts of circumferential wall and which certain eventualities, unless deliberately opposed, almost invariably tend to complete. Thus, axiomatically, the less a lacerated wound approximates the penetrating one—in other words, the fewer walls it has—the less likely its transition to a fistula; and the fewest walls a wound may have is one—a flat wound—hence the least likely to become fistulous.

Now all of this may sound too elementary, and indeed it may be common knowledge in the abstract; but, if so, at least the practical application as evidenced by the case reports betrays distortion and misconception. For example, the suturing of traumatic rectal wounds constitutes the most obvious, the most frequent and potentially the most serious violation of principle; and yet it is not only sanctioned but advised in printed word. Tempting but fallacious is the too prevalent concept that if sutures prove ineffective by virtue of wound infection nothing has been lost by the attempt. Fallacious, for it had been proved that healing is thereby delayed not moderately but far beyond that of wounds left wide open from the start. This time differential represents, in addition to the development and alleviation of confined infection, considerable tissue degeneration and sloughing. Such, however, is but the least disservice of suturing.

The consequences may be even more adverse than the stormy course of wound disruption, for apparent uneventful healing is too frequently the deceptive and vicious union of the more superficial parts only, with concomitant separation of the depths. By such "bridging," sutures have insidiously but effectively contributed the missing wall which we designated as the essential distinction between a lacerated and a penetrating wound, a lacerated wound and a fistula. The cure of such a fistula requires in essence the recreation of the original wound with healing by granulation—this time without benefit of suture.

But mismanagement by the use of sutures may have a graver conclusion than either explosive wound disruption or unvisioned fistulas compelling reoperation. Here I refer to the formation of fistulas either totally incurable or those necessitating at best far greater mutilation for cure than simple recreation of the original wound. There is intimation of such fistulas in the literature but little as to their pathogenesis or prevention or indeed as to just why they are incurable. One thinks

of the extent and relationships of a chronic fistula as being defined and limited by the pattern of the antecedent wound, of which the fistula is the direct residue. But as few traumatic wounds are in themselves incurable, whence then fistulas which transcend

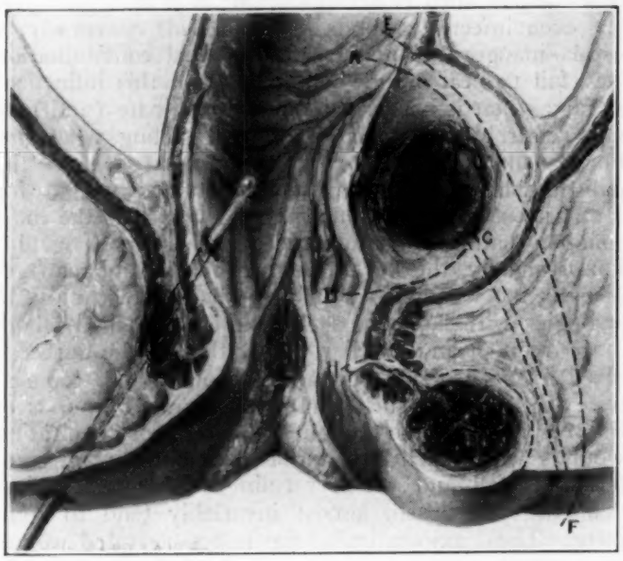

Fig. 1.—Composite drawing, illustrating several pathologic lesions: penetrating instrument and wound on the left, lacerated traumatic wound in the center with damage to the sphincter ani and perirectal abscess, right upper, such as occurred in case 1, following injury and suture of the rectal wall. Such an abscess, if taken early, should be curable by saucerizing within the arc of broken line *A-B*. If, on the other hand, spontaneous pointing to the skin is awaited, or if evacuative incision is made through the perianal skin as represented by line *C-D*, as done in case 1, saucerization of the large arc *E-F* becomes necessary. This means not only a dissection of far greater magnitude but also inclusion within its scope of the whole sphincter mechanism. Perianal abscess, right lower, of daily encounter, in contrast to the rare ones of truly rectal origin, commonly misnamed "rectal" abscesses (and fistulas). Adequate saucerization following perianal evacuation, as indicated by broken line *H-I*, rarely encompasses critical amounts of sphincter, again in contrast to the perirectal. This lesion is illustrated only for comparison and avoidance of possible confusion.

in both extent and complexity their own inceptive wounds? And just where and how does the attribute of incurability appear from the nowhere and affix itself? The unfolding answers spring from the fact that, while wounds may resolve directly and imperceptibly into chronic fistulas, acute and fulminating abscesses are a frequent intermediary stage between either a closed or a bridged wound and the final chronic fistula. This extension of pus under pressure may expand many fold the limits of the original injury and complicate its relationships, especially by reason of delays in diagnosis and procrastination of treatment which invariably attend abscesses in this area. In the superimposed disasters of preventable abscesses, then, are the inexorable and hardy seeds of the problem fistula. The first case report well illustrates the train of events attendant on suture of the lacerated rectal wall with the resultant abscess acquiring such relationships to the sacrum as to make it virtually inoperable (figs. 1, 3, 4 and 6).

What does all of this mean then—that traumatic wounds had best be idly neglected? To the contrary, aggressively active measures are usually necessary to counteract a unique local factor which of itself subserves the same treacherous union of superficial wound edges as established by sutures. This factor resides in a sort of collapsed status of tissues in the area, less readily described by word than by comparison in a way to the closed position of an accordeon, and is dominated both by the anal sphincter and by the natural apposition of buttocks and thighs. These influences must be anticipated by the conversion of wounds to as nearly as possible flat or "saucerized" forms, if need be through sacrifice of normal tissue. Such requirement may be moderated somewhat by persistent postoperative manual separation of the wound edges and/or by extended gauze packing, their necessity increasing in direct proportion to operative conservatism. The detriments of tissue loss are obvious; but on the other hand adequate manipulations and repacking of the wound are painful ordeals for the patient, requiring anesthetics and extra hospitalization so that even short of their absolute limits of effectiveness such measures approach the unpractical. The danger of incontinence by the prolonged separation of muscle ends through continued packing must be mentioned. The proper balance between tissue sacrifice and postoperative intervention—to gain the most for the least—is exclusively in the realm of individual experience, but I emphasize that in both particulars the occasional surgeon fails far on the side of insufficiency.

There are not only reasonable and relative limits to these complementary devices in assuring sound healing but there are absolute limits, which in summation define the real meaning of incurability. The restrictions to saucerization in the ischiorectal fossa are imposed by its walls, viz. the ischial tuberosity laterally, the urogenital diaphragm anteriorly and the anal canal medially (fig. 2). It is to be noted in contrast that the posterior wall is not as restrictive; being composed largely of fat, it can be generously removed. Furthermore, the slope of the pelvic floor is such that the attachment posteriorly is at about the same level as the apex of the fossa. This means that the latter, even to its uppermost point, may be well reached with at least a gutter carried posteriorly alongside the coccyx.

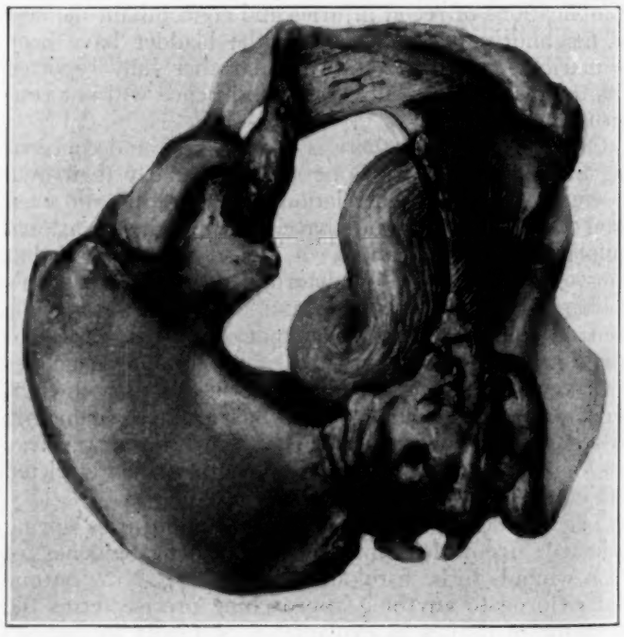

Fig. 2.—Anatomic structures having bearing on saucerization of wounds in the ischiorectal fossa. Restrictions are imposed by the ischial tuberosity laterally, the urogenital diaphragm anteriorly and the anal canal medially. The posterior wall, on the other hand, can be generously sacrificed. Furthermore the coccyx is at about the level of the apex of the fossa, owing to the hammock shape of the levator, which relationship also facilitates saucerization carried out posteriorly. Not only are these facts pertinent to the intelligent management of traumatic injuries but they are basic in the everyday treatment of spontaneous fistulas.

Deeper in the pelvis its bony walls impose obvious and impervious limits to saucerization (case report 1 and figs. 3, 4 and 6).

INJURY TO THE ANAL SPHINCTER

How does injury to the anal sphincter affect the issues? By no amount of sophistry can it alter or negate the principles established. The severed ends are but part and parcel of a wound which has innate potentialities for harm, and any compromise of management in their behalf either lacks cognizance of these dangers or else fears that suture alone assures continence and that all other contingencies are, or should be, subordinate.

To answer this in entirety would be but repetitious, except for dispelling the misconception of muscle suture as the sole safeguard against incontinence. The mind's eye, reverting to terms of probably more familiar experience, pictures the severed muscle ends behaving as those of long muscles which retract apart even to considerable distance. Such are not the particulars here, where both constrictive and splinting forces and constraints, which I cannot here pause to analyze, incline to maintain coaptation of the severed ends. This is constantly verifiable in fistulectomies both by direct observation and by clinical result, these controls being indeed so effective that the site of severance, particularly,

Fig. 3.—Problem fistula in case 1, either incurable or at best responsive only to excessively mutilative surgery. Represents the residue of an abscess following traumatic injury to the rectum which was treated as described in text and illustrated in figure 4. The main body of the fistula, found later to have extremely firm walls a half inch thick, lies on the hollow of the sacrum. At the extreme left is the barium filled rectum, while between can be seen catheter entering tract of previous perianal incision of the postoperative abscess, now communicating with both the rectum and the main body of the fistula.

must be watched for bridging. That there is of course a limit to this reserve goes without saying. Suturing only the ends of a severed sphincter (fig. 5 and case 2) is a furtive synthesis of half-truths, combining a half-hearted open wound and recollected pictures of plastic repair. While not impossible of result by the expert, it bespeaks more likely a credulous naïveté which has stumbled onto a hard way of doing things when even the easier exceeded the surgeon's capability. Union of the ends is the most facile contribution toward bridging, which immediately implies (1) more radical treatment and expert management of the rest of the wound to prevent it too resolving to a fistula and (2) later severance of the union on the principle of a two stage fistulectomy. And why sutures in the classic repair of the incontinent sphincter if so ill advised in its immediate restoration? Too briefly for all the facts: (1) In the one case muscle recovery has reached equilibrium while in the other an advanced degree of improvement is in prospect and (2) the surgically created wound is controllable (*a*) in extent and (*b*) in site wholly outside of, and separated from, the anus. These admit of a more tractable pattern of nonfistulous character holding brighter prospects of sound healing and, at the worst, disruption to the status quo. Even so, this operation in such a soiled field is a compromise with the ideal, as

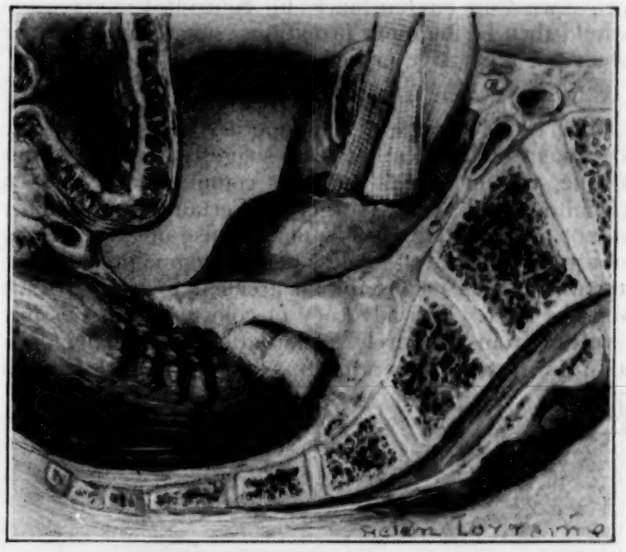

Fig. 4.—Method of treatment by surgeon in case 1. The important point is suture of the traumatic laceration of the rectum, which I hold to have been inadvisable. Drain carried from rectum through rent in peritoneum and up through abdominal wall. Several weeks later a retrorectal abscess formed which was opened through perianal skin (fig. 1), resulting in condition shown by x-ray in figure 3; such incision also is objectionable for reasons given in text and illustrated in figure 1.

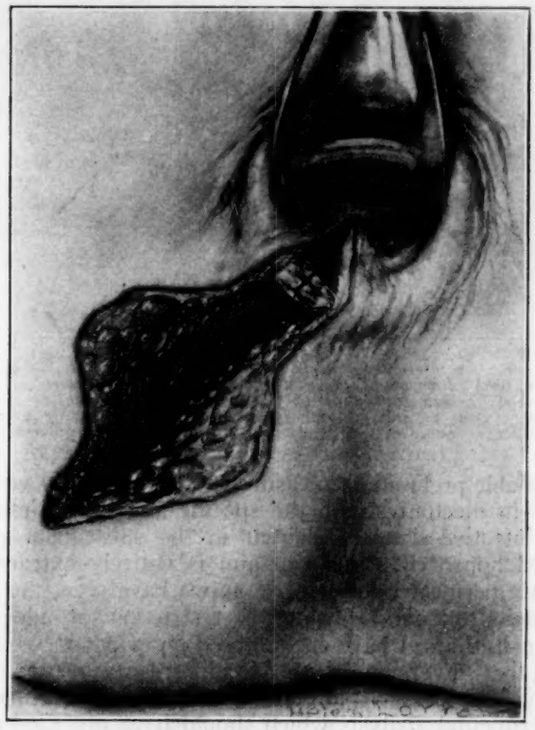

Fig. 5.—Treatment by surgeon in case 2. Only the severed sphincter ends were sutured, leaving the rest of the wound untouched. If the sutures slough, they serve no object; if not, a fistula of the whole wound is almost inevitable. If in addition the wound had been adequately saucerized, the sphincter possibly could have been severed later if the sutures held—on the principle of a two stage fistulectomy.

results compiled and reported by us elsewhere prove;[2] it is for this reason that in previous papers on elective

2. Blaisdell, Paul C.: Repair of the Incontinent Sphincter Ani, Surg., Gynec. & Obst. **70:** 692, 1940. Blaisdell, Paul C.: Repair of the Incontinent Sphincter Ani, ibid. **75:** 634, 1942.

repair I included suggestions of a vaginal approach more wholly consonant with logical principle.

The traumatically injured sphincter should be simply left alone, thereby taking full advantage of its own capacity of spontaneous recovery; if later this should prove wanting, circumstances for controlled intervention would then be far more propitious, safe and with wider choice of reparative procedure.

TEMPORARY COLOSTOMY

The establishment of a temporary colostomy in the treatment of injuries has been suggested, and, it seems to me, without critical analysis commensurate to such circuitous and radical surgery. Certainly a colostomy is not a preventive of a fistula because of the time lag of attributable effect—unless perchance one prepares the rectum by this means for an accident to happen some months later. The advocacy of colostomy has possibly evolved from the careless translation of special indication into more general terms—for example, from a

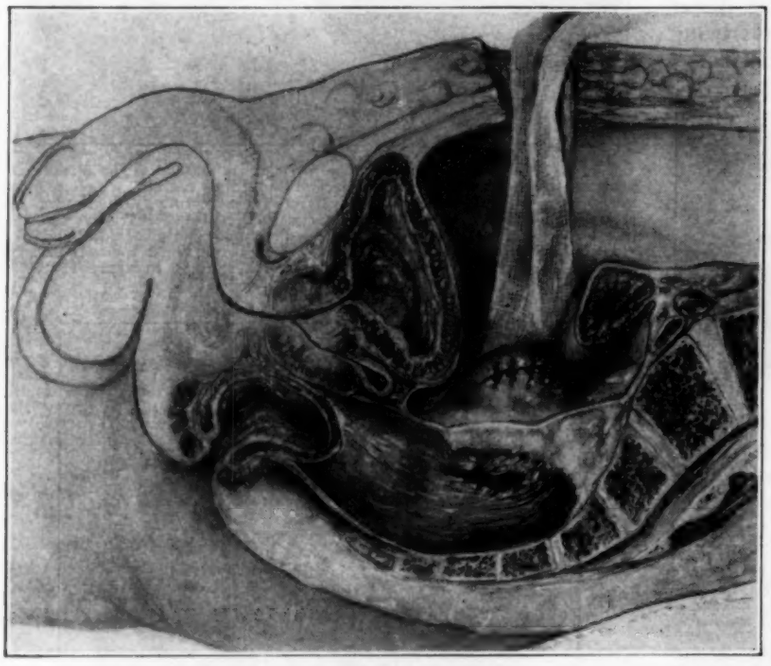

Fig. 6.—An alternative method of treating case 1 which, I suggest, is preferable to the one used as shown in figure 4. The peritoneum is sutured and the rectal rent left unsutured: indeed as healing of the lower wound progressed it might have proved expedient even to enlarge—rather than suture—this opening to insure saucerization. The abscess, source of the fistula, might thus have been prevented.

justifiable preliminary measure for a complicated vesicocolic fistulectomy, with the specific aim of minimizing the infective danger inherent in the subsequent peritoneal approach. Such an aim is entirely extraneous to any perineal issue, where, as we have seen, the sole obstacle to sound healing is restriction of adequate saucerization. I have encountered no evidence to establish that diversion of the fecal stream is a counter equivalent to such limitation—a point susceptible to experimental analysis which should have preceded clinical application. And there is considerable evidence to the contrary, such as in the behavior of recurrent pilonidal sinuses; for here, likewise, unsound healing is due far above all else to faulty wound architecture (shown by the fact that the recurrence rate is twenty times greater in sutured than in open wounds [3]) and yet devoid of any fecal stream influence, not belatedly effected either, as in the case of colostomy for wounds under discussion, but absent from the very inception.

There are objectionable possibilities in a temporary colostomy from a false sense of security induced. Indeed the test and criterion of management is the behavior and progress of the wound under what are to be its permanent environments.

TREATMENT OF THE INTERMEDIARY ABSCESS

If and when an abscess has been allowed to form (case 1), does there still exist any choice of management or should incision invariably be made perianally as well-nigh universally advised? The time element holds the key to the situation not only in minimizing both the progressive extent and the cumulatively complex relations outlined but also in offering any choice as to locus of incision. (By such choice I do not refer to direct incisional damage to the sphincter, although in a series of cases of incontinence that I compiled an incredible proportion were the result of simple incision of perianal abscesses.[4]) It must be admitted that procrastination usually settles all issues by unimpeded pointing of the abscess, but this does not prove that something better is impossible. The significance of the incisional site stems from the fact that the course of any incision becomes itself an integral part of the residual fistula, so that to this extent the relationships of the latter are determinable. With an abscess of intrarectal origin this in itself may make the whole difference as to whether the entire sphincter mechanism becomes involved or spared in the subsequent fistulectomy, with vital bearing on continence. Figure 1 portrays the theoretical background of this principle, as case 1 establishes the pragmatic and sober actuality.

This must not be construed of course as advice for the incision of the common perianal abscess of anal as distinguished from rectal origin, whose arc is so largely determined by embryonic anal ducts as rarely to include critical amounts of muscle, as also illustrated.[5]

REPORT OF CASES

The following are 4 consecutive cases of traumatic injury, with 3 illustrating points of mismanagement:

Case 1.—A youth aged 18 entered the hospital directly following an accident in the mountains. Sliding downhill on a rubber coat he had collided with a sled, the steel runner of which penetrated upward through his rectum. Pronounced rigidity of the abdomen was the essential indication for immediate laparotomy by his attending surgeon. Through a midline incision exploration disclosed a rent in the pelvic peritoneum close to the iliac vein, and a small piece of raincoat near this opening was removed. The hole in the rectum was sutured, the pelvis cleaned, a drain carried to the rectum through the peritoneal defect and the abdomen closed around the drain (fig. 4). The latter was removed gradually over a period of days as drainage ceased.

Three months later the patient was readmitted because of septic fever of unstated duration and a large retrorectal abscess evacuated by a perianal incision lateral to the rectum (fig. 1) and the original traumatic tear of the rectum which had failed to heal was resutured. Coincident with healing of the perianal

3. In a compilation of over 4,000 cases of pilonidal sinuses submitted by members of the American Proctological Society, Kleckner found recurrence to be twenty times more in closed wounds than in those left wide open. This proves that recurrence is a matter of wound architecture and not of incomplete removal.

4. Blaisdell, Paul C.: Pathogenesis of Anal Fissure and Implications as to Treatment, Surg., Gynec. & Obst. **65**: 672, 1937.

5. Blaisdell, Paul C.: The Origin and Treatment of Anorectal Fistulae, California & West. Med. **49**: 6, 1938.

incision septic fever gradually returned, at which time the patient was referred to me. An x-ray film taken at this time is shown in figure 3.

Under gas anesthesia a belated attempt was made to saucerize the complicated fistula, leaving until later the problem of its encirclement of the whole sphincter mechanism. The patient was in good condition on leaving the table but within a few minutes became suddenly cyanotic, with labored breathing, and died within a few minutes before I reached his room. A postmortem was performed by Dr. Allvyn Foord, who ascribed death to massive collapse of the left lung. The abscess cavity in the hollow of the sacrum was found to have a wall of dense and extremely hard fibrous tissue 1 to 2 cm. in thickness, and only by sharp dissection with a heavy knife could it be stripped from the underlying bone. A far more radical operation than I had attempted would have been necessary for cure, if even possible.

Suture of the rectum was an invitation to a retrorectal abscess impossible of saucerization through the abdomen; inevitable sloughing of the sutures converted the abscess to a blind fistula. Resuture of the rectum across an abscess cavity is and was pointless, and perianal incision vastly complicated any possible cure of fistula, as explained in figure 1; instead, intrarectal saucerization should have been attempted. (See also figure 6.)

CASE 2.—A boy aged 10 years entered the hospital several hours following an impalement injury of the rectum suffered by falling on a picket fence. He was assigned to a general surgery service, where, in the absence of signs or symptoms of peritoneal encroachment, the lacerated sphincter ends were united by interrupted sutures; the remainder of the wound was simply left alone (fig. 5). After a period of several months the patient was referred to the rectal service because the wound continued to drain. On examination under anesthesia a deep fistula was found to occupy the entire original wound, necessitating fistulectomy by its recreation and saucerization, allowing it then to heal from the bottom by granulation. There was no residual muscle weakness.

This patient was forced to repeat surgery and weeks of convalescence because of mismanagement. Simply leaving the wound open was not sufficient to preclude fistula formation, additional saucerization being indicated. Suture of the muscle increased the likelihood of a fistula and served no useful purpose.

CASE 3.—A man aged 30 suffered an impalement injury of the rectum in an automobile accident, the details of which were not remembered by the patient. He was removed to a hospital near the scene and the whole wound closed with interrupted sutures, after which the patient was sent to me. After several days the wound broke down so badly that reoperation became immediately necessary; all sutures were removed and saucerization, which should have been carried out at the original operation, was now established.

If sutures hold, abscesses or fistulas and reoperation usually result as illustrated in cases 1 and 2; if ineffective, as here, they are also worse than useless, occasioning at best unnecessary surgery and delayed convalescence.

CASE 4.—A man aged 30 was thrown from a skidding motorcycle. He was assigned to the orthopedic service, where it was determined that he had suffered a broken humerus, femur and pelvis; I was consulted about a large gaping wound of the perineum entering the rectum. The patient was complaining of abdominal pain, but no rigidity was determinable. Immediate examination of the wound was carried out under anesthesia, and extension through the peritoneum was definitely ruled out. Even though it was already a large wound, much tissue was further sacrificed to obtain certain saucerization; this was particularly necessary because the other injuries would interfere with continued postoperative manipulation. Within a few days granulations made the wound quite insensitive and it required almost no care. The sphincter, although more than halfway severed by injury, healed without any loss of control.

Here is demonstration of conformity to logical principle.

102 North Madison Avenue.

LESIONS OF THE MUSCULOTENDINOUS CUFF OF THE SHOULDER

2. DIFFERENTIAL DIAGNOSIS OF RUPTURE

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NEW YORK

The most adequate present guide to the diagnosis of rupture of the short rotator cuff of the shoulder is outlined and described in detail by the late Dr. E. A. Codman in his classic text "The Shoulder." [1] In considering the diagnostic aspects of rupture he frankly admitted that he never had had the opportunity to study a fresh case. He then went on to postulate eighteen conditions which he thought ought to be fulfilled before a positive diagnosis of early rupture should be made. His clinical syndrome was a rather exacting one which, in spite of its hypothetical nature, came surprisingly close to the mark. However, since the publication of his book a considerable number of proved ruptures, both early and late, have been studied by the Fracture Service of the Presbyterian Hospital in New York and certain modifications of and additions to this syndrome seem indicated.

The requirements for diagnosis of a cuff tear differ little if any from those of a tear in any other tendon or tendon group. They include:

1. A detailed history characterized by compatible subjective symptoms.
2. Demonstration of absent or deranged function in the structure involved.
3. Supportive evidence in the form of local signs compatible with damage to the structure involved.
4. Elimination of other conditions requiring differentiation.

HISTORY AND SYMPTOMS

Codman stipulated that the patient be a laborer past 40. Sixty proved ruptures form the basis of this report. Eleven were under 40. Five were under 30. Nineteen were in women, most of whom could not be classed as true laborers. It is evident that, while most ruptures occur in well used shoulders past middle age, the incidence of the lesion is by no means restricted to this age and group. Codman's statement might well be modified to say that the cuff in any laborer past 40 is sufficiently scarred and degenerated by repeated minor traumas and attrition that it ruptures with relative ease.

He stipulated that the history include an adequate trauma, usually a fall. If by this he meant trauma adequate to rupture a weak and degenerated tendon his hypothesis has been corroborated. Almost but not

Read before the Section on Orthopedic Surgery at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

From the Fracture Service of the Presbyterian Hospital in New York, and the Department of Surgery, Columbia University College of Physicians and Surgeons.

1. Codman, E. A.: The Shoulder: Rupture of the Supraspinatus Tendon and Other Lesions In or About the Subacromial Bursa, Boston, privately printed, 1934.

all patients date the onset or aggravation of symptoms from an injury of some sort. Few such injuries are serious in the ordinary sense of the word and many are minor enough so that they fittingly might be called inadequate. At times the most detailed history fails to uncover any trauma at all. An interesting characteristic of the pathologic condition found in the latter group is the presence of extensive fibrillation and degeneration of the tendon substance at the point of rupture not unlike that occasionally encountered in ruptures of middle aged achilles or quadriceps tendons. It seems reasonably certain that extensive degeneration at times so weakens the tendon substance that it may rupture without significant cause.

The rupture, whether spontaneous or the result of trauma, is accompanied by a sudden sharp pain in the shoulder. The patient often describes a sensation of something snapping or giving way. From this time on the history and symptoms generally follow a fairly consistent pattern. The primary pain is momentary and usually passes off, only to recur within a few hours. The quiescent period apparently represents the time necessary for the torn tissues to become swollen and inflamed so that their easy passage under the acromion and coracoacromial ligament no longer is possible. Once it is over, pain and spasm are continuous, aggravated by motion of the arm and especially those motions causing the torn portion to brush against the overlying bone or ligament. For the first few days the pain progressively increases in severity, reaches a peak and then gradually subsides. In many cases it subsides completely. In most cases it eventually reaches a level of severity at which it remains more or less constant and at which it may or may not result in sufficient disability to warrant radical therapy.

A definite diagnosis usually is impossible in the presence of acute pain which precludes adequate functional evaluation of the various muscular and ligamentous components of the shoulder. It is considered that no definite diagnosis, prognosis or radical treatment is warranted during the stage of acute pain. This is in direct variance with Codman's plea that such ruptures be diagnosed and repaired at an early date. He made this plea in the hope that early repair would be easier to do and might be followed by better and more speedy recovery. The following reasons substantiate the conviction that early repair is not warranted in the average case:

1. Early repair has been no easier to accomplish than late.

2. The results of early and late repair have been identical both for time and for completeness of recovery in comparable cases.

3. The symptoms in a large percentage of cases showing a clearcut clinical picture of rupture subside spontaneously under conservative therapy to such an extent that repair never need be done.

4. The rupture almost invariably takes place through a degenerated portion of the tendon. As a result, speedy and efficient union of the repair can be expected only after the degenerated edges of the tear are excised back to healthy tendon tissue. The rupture therefore is the equivalent of an old lesion as soon as it occurs, and whether operated on early or late excision and revision of its periphery is equally necessary.

The acutely painful stage usually commences to subside a week or so after the onset. When this occurs pain is replaced by actual weakness or inability in elevation of the arm as the predominant subjective complaint in the larger tears, and by minor derangements of function characterized by acute catches of pain in certain positions in the lesser lesions. A constant ache referred to the region of the deltoid insertion frequently persists in addition to the other symptoms. Usually at least two and not more than four weeks after the onset the painful symptoms are found to have subsided sufficiently so that a detailed functional examination is possible.

DEMONSTRATION OF ABSENT OR DERANGED FUNCTION

The function of the musculotendinous cuff is intricate and difficult to comprehend except on a basis of living anatomy. Its power of rotation is obvious. Cases with deltoid paralysis have indicated that abductor power, although present, is weak and inefficient when it acts alone. Codman has given a comprehensive description of its anatomy and physiology and emphasized its importance as a stabilizer of the glenohumeral fulcrum during abduction of the arm. Inman, Saunders and Abbott [2] emphasized and evaluated the relative importance of the various muscles with respect to their place in maintaining the muscle force couple of the shoulder mechanism. A retrospective study of a considerable number of cases with proved ruptures involving various segments of the cuff, and a correlation of the operative findings with detailed preoperative functional evaluations, have resulted in some additional useful observations.

The musculotendinous cuff consists mainly of the four intrinsic muscles of the shoulder whose origins arise from divergent points on the scapula and whose tendinous portions converge and fuse to form a continuous envelop enclosing the anterior, superior and posterior aspects of the humeral head and to insert into the bone at the region of its anatomic neck and tuberosities. The subscapularis portion of this common insertion attaches to the lesser tuberosity, the supraspinatus, infraspinatus and teres minor portions respectively to the anterior, middle and posterior facets of the greater tuberosity. The subscapularis is joined to the suprasinatus by an aponeurosis through which the fibers of the two tendons decussate.

It is a widely accepted belief that supraspinatus function constitutes an essential factor in the initiation and maintenance of abduction against gravity. Operative findings have proved this belief to be unfounded. Almost if not all patients with complete rupture of the supraspinatus alone have been able to initiate and maintain abduction of the extremity prior to repair. Larger tears involving more than one whole tendon have been found to retain these two functions in certain planes of humeral rotation and lose them in others. Complete avulsions of all the cuff insertion have shown a complete absence of power to initiate or maintain elevation in every plane of humeral rotation. Therefore it seems certain that although function of the cuff unit is essential to the initiation, performance and maintenance of elevation, that of the supraspinatus or any other individual member is not. It has been apparent that small ruptures such as those involving the supraspinatus alone are compensated for, when necessary, by the remaining intact attachments on either side, in

2. Inman, V. T., Saunders, J. B. deC. M., and Abbott, L. C.: Observations on the Function of the Shoulder Joint, J. Bone & Joint Surg. **26**: 1-30 (Jan.) 1944.

the same way that intact vastus expansions compensate for the function lost with certain undisplaced patellar fractures.

The cuff, irrespective of the individual tendons involved, is divisible into anterior, superior and posterior segments as it embraces the humeral head (fig. 1). The anterior and posterior segments exert a rotary force. Their lower components exert what Inman, Saunders and Abbott have aptly termed a depresser force on the humeral head, although clinical findings do not entirely substantiate their estimate of the importance of this force in the act of elevating the arm. All three pull the humeral head against the glenoid. The superior segment has an additional mechanical advantage such that it exerts an abduction force on the humerus, acts as a depresser up to 90 degrees and past this point helps to suspend the humeral head against gravity. The particular tendon or tendons making up this superior segment depend on the rotational position of the humerus. In external rotation it is made up of the subscapularis and supraspinatus, in neutral by the supraspinatus and the anterior portion of the infraspinatus and in internal rotation by the infraspinatus and at times the teres minor (fig. 1). Operative findings correlated with preoperative functional defects have demonstrated clearly that the function of the tendons making up the superior segment in any given position of humeral rotation is the essential factor in both initiation and maintenance of abduction and that the function of the individual intrinsic muscles is interchangeable in this respect, depending on the position of the humerus and the plane of motion.

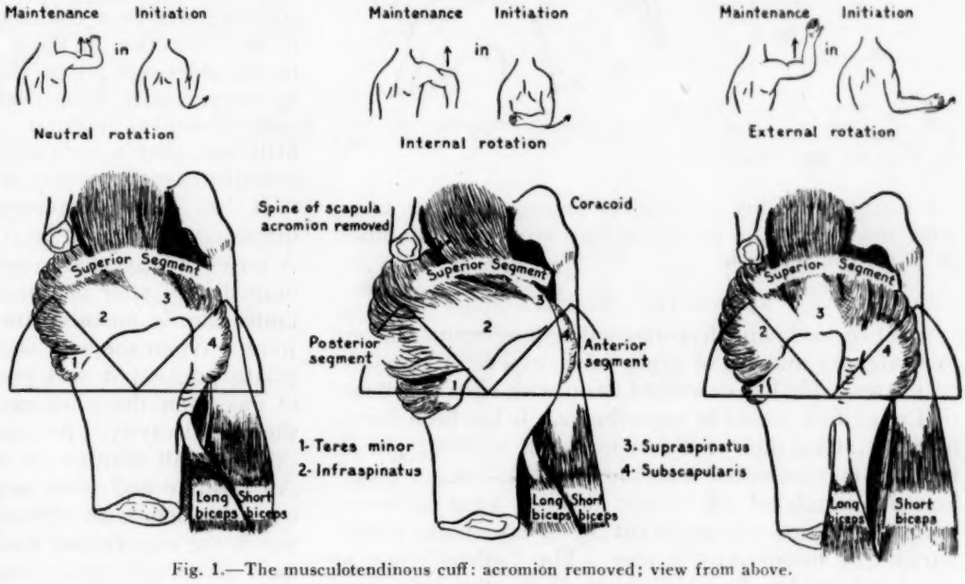

Fig. 1.—The musculotendinous cuff: acromion removed; view from above.

Knowledge of this fact makes possible an adequate functional evaluation, not only of the cuff as a whole, but also of its individual components. In the routine examination of shoulders it is considered essential that initiation and maintenance of abduction be tested in all planes of humeral rotation before deciding that the intrinsic muscle cuff is functionally intact. When a certain tendon is suspected of rupture the humerus is rotated until the suspicious area is brought into the position of greatest functional demand, i. e., brought to occupy a position in the superior segment. Evaluation of initiation and maintenance then denotes the functional efficiency of the suspected area alone. Tests for maintenance of abduction give more definite reactions and are more reliable than those for initiation, which, as Inman, Saunders and Abbott have pointed out, is quite variable.

The reactions to all functional tests are brought into sharper focus when the examiner opposes the function with manual or other resistance.

The technic of functional evaluation is simple. In order to test initiation of abduction the flexed elbow is held against the side by the examiner and the patient is required to attempt abduction against this manual resistance in one plane of rotation after another until the complete range of rotation has been covered. Maintenance of abduction is tested by passively abducting the arm to 90 degrees, following which the patient, after first relaxing all muscles, is required to maintain the abducted position against both gravity and downward pressure by the examiner. All planes of rotation must be tested.

Confirmation and support for these functional tests may be obtained by having the patient attain full elevation in the position of quadruped extension, which is always possible. Then with a little help and by straightening up from the stooped position it will be found that maintenance of complete elevation in the erect position is also possible. But as the patient commences to lower the arm, thereby creating a functional demand for glenohumeral stabilization by the cuff, it will fall helplessly to the side if a gross tear is present, again provided the plane of humeral motion is such that the torn portion occupies the superior segment.

Interpretation of the reactions to such tests is not difficult when approached with a comprehension of several facts which commonly tend to confuse the picture:

1. No functional test is valid until the acutely painful phase subsides sufficiently so that pain does not interfere with muscle action (usually a matter of about two weeks).

2. All persons suffering from rupture quickly learn to initiate and maintain elevation by rotating the arm into a position such that the remaining intact cuff occupies the superior segment.

3. No rupture, with the exception of a complete avulsion, can be identified by demonstration of localized absence or derangement of function until the arm is rotated into a position creating functional demand on the ruptured portion.

4. Incomplete and small complete tears are characterized by pain limited to those rotational positions creating a functional demand on the injured portion. Localized weakness may be present but is seldom noticeable enough to be appreciable.

5. Ruptures up to 1 inch in length frequently are compensated for by the adjacent cuff attachments. The reaction to functional evaluation under such circumstances is weakness and pain localized to the appropriate segment of the rotation arc, producing a functional demand on the injured part.

6. Localized inability to maintain abduction against two finger resistance denotes loss of function in an appreciable portion of the cuff and usually a tear of at least 1 inch or more in length.

7. Localized inability to maintain abduction against gravity denotes a large tear usually involving the equivalent of two whole tendons.

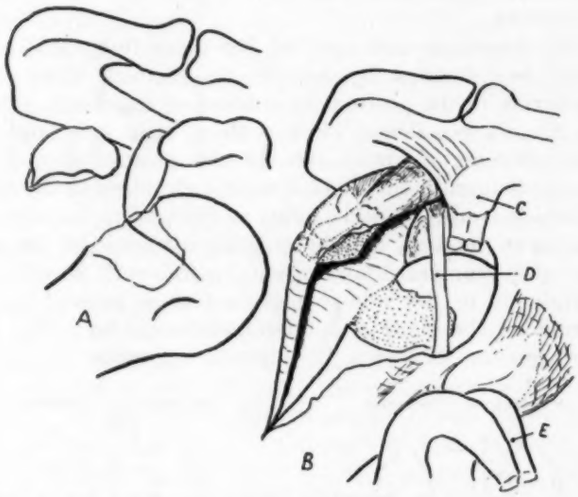

Fig. 2.—Dislocation with unretracted tuberosity fragment: *A*, x-ray; *B*, anatomic sketch; *C*, coracoid; *D*, biceps tendon; *E*, reflected coracobrachialis and short biceps head.

8. Complete inability to initiate or maintain abduction in any plane usually denotes a massive avulsion involving all or almost all of the cuff insertion.

SUPPORTIVE EVIDENCE

Most of Codman's hypothetical requirements fall into this category and are of great value, especially in equivocal cases. He has described them with such excellence that repetition would be superfluous. It has been found, however, that their evaluation is not without pitfalls for the inexperienced examiner. His "tender point" may be simulated by calcific deposit, local infection, minute fracture not apparent by x-ray, bone tumor, bursitis or minor muscle tear. The "sulcus" may be simulated by bundles of deltoid fibers, the long head of the biceps or a thickened redundant bursal roof. Palpation of the greater tuberosity through an atrophic deltoid demonstrates an excellent "eminence" even with an intact cuff. The "jog and wince on motion" are encountered frequently with subacute or chronic calcific deposits. "Palpable crepitus on motion" is an excellent and important sign but not until one learns to appreciate the difference between the crepitus produced by chronic inflammatory thickening in the bursal wall and that produced by palpation of a mobile tab of torn tendon. "Faulty scapulohumeral rhythm" is present in all painful shoulders regardless of cause. "Little if any restriction when stooping" is constantly true of ruptures but is also true of certain other minor traumas simulating the clinical picture of a tear. "No painful symptoms prior to the accident" was a constant history in Codman's cases. In about 50 per cent of the proved ruptures in the present series symptoms were complained of prior to their accident, and this was understandable in that many of them were found to have a recent extension superimposed on an old tear.

Muscle atrophy and atony constitute an important differential sign, as Codman also pointed out. General disorders of the shoulder usually result in atrophy of the deltoid. Disuse results in diffuse atrophy, most apparent in the deltoid. Rupture of the cuff results in selective atrophy of the involved intrinsic muscle or muscles unaccompanied by a corresponding deltoid myopathy. This phenomenon becomes appreciable to both inspection and palpation between the ends of the second and third weeks and contributes important evidence in support of the diagnosis. Bursal disorders produce deltoid atrophy without a corresponding change in the bellies of the intrinsic rotators.

Codman required a negative x-ray as one of the conditions to be fulfilled. Exception must be taken to the literal implications of such a flat statement. Ruptures not uncommonly occur in conjunction with other bone and joint lesions and, although they may be the most disabling lesion present, are prone to be missed when attention is distracted by the obvious bony pathologic change evidenced by the x-ray film. Roentgen examination not only is of great value in ruling out other simulating conditions but often supplies supportive and, at times, pathognomonic evidence of a torn cuff. Early ruptures, especially in younger persons, are apt to be characterized by a completely negative x-ray. Ruptures of long duration or those resulting from minor trauma in the older age group almost always are characterized by degenerative bone changes in the tuberosity at the point of tendon avulsion. Such a finding in itself means little but, when accompanied by compatible clinical signs, constitutes real evidence in support of the diagnosis.

It has been demonstrated that a positive clinical diagnosis of tear can be confirmed by roentgenography. A series of suspected cases was examined by fluoroscope immediately after injection of 50 cc. of filtered oxygen under sterile auspices into the cavity of the shoulder joint. When the arm was manipulated into the appropriate position it was possible to visualize the escape of gas from the joint cavity through the rupture into the bursal cavity. No such phenomenon was observed in the small number of controls used for comparison. All positive and some negative results were confirmed by operation, and although the number of cases in which the experiment was done was small its efficiency as a diagnostic procedure seemed reasonably certain.

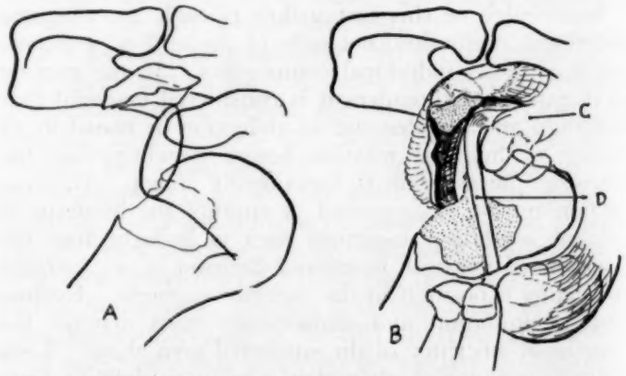

Fig. 3.—Dislocation accompanied by retracted tuberosity fragment: *A*, x-ray; *B*, anatomic sketch; *C*, coracoid; *D*, long head of biceps.

Subsequent improvement in the methods of functional evaluation have made any such test, accompanied as it is by a potential risk of infection, unnecessary.

Roentgen examination is most important in the diagnosis of ruptures associated with fracture or dislocation. Not uncommonly a torn cuff is the most disabling factor in a complex shoulder injury. Usually clinical identification of the rupture is impossible until long after

the bony lesion has healed. Frequently a positive roentgen diagnosis is possible at the first examination.

Dislocation at the shoulder accompanied by a fracture of the greater tuberosity (69 times in 439 dislocations in the records of the Presbyterian Fracture Clinic) almost always is accompanied by a torn cuff. Most such tears do not require operative repair, but others result in serious disability unless attended to.

They may be divided into three main groups, each of which can be identified by x-rays taken prior to reduction of the dislocation.

The largest group requires no operative intervention. It includes all those cases in which the tuberosity fragment conforms to the position indicated in figure 2, neither retracted up under the acromion nor pulled downward as far as the dislocated humeral head. The anterior joint capsule usually has been found to be intact and the dislocation to be essentially intra-articular. The abnormal position of the humeral head results from an avulsion of all its superior and posterior attachments as indicated in the anatomic sketch. Reduction of the dislocation results in anatomic reposition of the tuberosity fragment and also of the edges of the longitudinal cuff rent so that no repair is necessary.

The second group includes those cases with the tuberosity fragment retracted up under the acromion as depicted in figure 3. Such a film constitutes definite evidence of a large tear across the cuff (without which no such retraction is possible) and usually a massive avulsion of the cuff from the humeral head as indicated in the anatomic sketch. Early repair is essential to a good result.

The third group includes the cases wherein the tuberosity fragment is pulled downward and remains relatively unseparated from the humeral head (fig. 4). Such a lesion may correspond to the "false dislocation" described by Codman, and when this is the case a lengthy rim rent or deep surface tear commonly accompanies the dislocation and may result in delayed or incomplete recovery. At times the pathologic change of the soft parts consists of a small longitudinal rent and an avulsion of the posterior capsule or glenoid labrum as indicated in sketch 2 in addition to an anteroinferior capsular tear. Occasionally there is an avulsion of the cuff attachments from the tuberosity as in sketch 3. The latter condition may be suspected when reduction of the dislocation is accompanied by a failure of the tuberosity to resume its normal anatomic position.

Certain dislocations are reduced when first seen. Incomplete reduction or persistent subluxation of the humeral head, even if only slight in amount, usually is indicative of a large tear and in an elderly person, especially if degenerative changes are apparent in the humeral head, is almost pathognomonic of a complete cuff avulsion.

OTHER CONDITIONS REQUIRING DIFFERENTIATION

A rupture of significant size resulting in demonstrable functional derangement produces a clinical picture not closely simulated by any other condition. Small complete or incomplete tears resulting in equivocal functional defects often require differentiation from the following conditions:

1. Painful calcific deposits. These may be identified by adequate x-ray films. More than a hundred deposits have been explored. Only one was accompanied by a torn tendon. Therefore it seems reasonable to assume that the presence of a calcific deposit makes a rupture in the same shoulder highly improbable.

2. Minor fractures, especially undisplaced fissures in the greater tuberosity, which usually may be identified by x-ray.

3. Rupture of deltoid or intrinsic muscle fibers. Either may produce signs and symptoms suggestive of a small rupture in the cuff, and this seems especially true in younger persons. Four patients under the age of 30 have been subjected to exploration for the purpose of doing an early repair of a torn cuff in whom the pathologic change consisted of a hematoma in the under surface of the deltoid and in 1 case of the belly of the supraspinatus. A minimum of two weeks' delay before deciding on operative intervention greatly minimizes the risk of this mistake.

4. The so-called "frozen shoulder." No tear has been encountered in exploration of a stiffened shoulder, and none of the 60 proved ruptures presented had any significant limitation of passive motion.

5. Certain forms of chronic bursitis characterized by inflammatory thickening of the bursal roof, which is thrown into folds on motion of the arm. The result is an internal derangement of the articulation between cuff and acromion or acromial ligament, and the clinical picture produced is difficult to differentiate from that of a small tear. Exploration and excision of the bursa constitute not only the final differentiation but also the most efficient therapy for the condition.

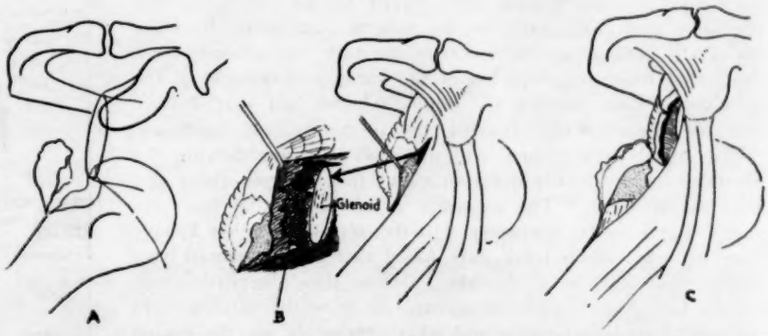

Fig. 4.—Tuberosity fragment pulled downward and remaining relatively unseparated from the humeral head: *A*, x-ray; *B*, interior of joint cavity, posterior capsule avulsed from glenoid labrum allowing tuberosity to follow humeral head; *C*, avulsion of cuff tendons allowing tuberosity to follow humeral head.

INDICATIONS FOR OPERATIVE THERAPY

Establishment of a positive diagnosis does not afford adequate indication for operation. The symptoms and disability resulting from many ruptures subside spontaneously. At least half the patients in whom an early diagnosis of rupture has been made in our clinic have maintained the signs but eventually lost most of the symptoms of the lesion. Almost all have been adequately followed, and it has been apparent that, while such subsided lesions may produce occasional mild symptoms related to weather or overuse, no disabling exacerbations of pain are liable to occur unless the shoulder is subjected to another injury.

The only definite indication for operation consists of pain or disability sufficient in duration or severity to make the procedure worth while from the patient's point of view. This indication may exist in the presence or absence of a clearcut diagnostic picture. Even in the absence of definitive signs the diagnosis of internal derangement of the shoulder joint may be made and, as in the case of the knee joint, warrants exploration and eradication of existing pathologic conditions.

SUMMARY

Under the auspices of a plan for diagnosis and evaluation of the torn shoulder cuff, 64 shoulders were explored with a preoperative diagnosis of rupture. The diagnosis was incorrect in 4 cases.

180 Fort Washington Avenue.

ABSTRACT OF DISCUSSION

DR. JAMES E. M. THOMSON, Lincoln, Neb.: It is rather interesting that within the course of a single year there should have been brought into the literature and to you today such epochal discussions involving a new and revolutionary understanding of these shoulder cuff lesions. I refer to the recently published work of Inman, Saunders and Abbott and also to that of Dr. David Bosworth and now to the author of this paper: in particular, to their anatomic understanding of the function of the shoulder, in the first instance, and secondly the surgical approach and the possibilities of operative repair. Lastly this paper by Dr. McLaughlin contributes significantly to the diagnosis and indications for operation. This is one condition in which there is no hurry about operation. Usually a pathologic condition has existed for a long time prior to the injury, and we can take time to study the possibilities of its future and its repair. Dr. McLaughlin has brought out some very pointed observations with regard to the indications for operation and particularly to the fact that an early diagnosis cannot be made, that evaluation of the tear can be made by a functional rotary examination of the various movements of the shoulder. Since hearing the author's paper last year I have had the pleasure of following his procedure and approach. Those to whom it is new will find that they are viewing the shoulder from a totally different view; that is, from above and into the shoulder. The exposure is so broad that one sees much that may be confusing. In the series in which I have operated tremendous tears were found that I never would have thought possible in a shoulder. From this observation one cannot but wonder whether perhaps many of the smaller tears do not heal spontaneously and whether that is not the reason one feels that it is appropriate to wait until one makes a positive diagnosis before operating. I am still confused in trying to make an accurate diagnosis because I have not been able to demonstrate the small tears, but I have had great satisfaction in using this exposure and repairing satisfactorily massive tears of the shoulder cuff. This paper is epochal in its subject matter and the understanding of this very complex problem of internal derangement of the shoulder.

DR. EDWIN W. RYERSON, Chicago: The first thing that struck me in reading the paper was the probability that the women of Boston are a little bit tougher than the women of New York, because Codman never reported this injury in any women. Also that probably the New York women belong in the class of laborers more than the ones in Boston do. I have not seen this happen in any women except one whom I saw two weeks ago who fell from a horse and had ruptured part of her musculotendinous cuff. The other important point was the careful consideration given by Dr. McLaughlin to the nonoperability of so many of these cases, and it is true that many of them, especially in older people, are the result of a degeneration of the musculotendinous cuff due to age, occupation and arduous work. If one tries to repair these tears one does not, as a rule, get a very good result. I am less and less in favor of operating on the older people with the degenerative tendency.

DR. HARRISON L. MCLAUGHLIN, New York: Dr. Thomson has brought up the question of the diagnosis of small and incomplete ruptures. I know of no method for their certain diagnosis. This paper was based on a series of cases preoperatively diagnosed as rupture and in most of them there were fairly extensive lesions. In many other cases exploration has been done in our clinic with a preoperative diagnosis of internal derangement of the shoulder, and it has been in this group of cases that most of the small and incomplete ruptures have been encountered.

THE TREATMENT OF EMPYEMA THORACIS WITH PENICILLIN

CAPTAIN MARTIN J. HEALY JR.
AND
CAPTAIN HARRY L. KATZ
MEDICAL CORPS, ARMY OF THE UNITED STATES

The recent advances in the therapy of pneumonia with the sulfonamide compounds have reduced the frequency of the dreaded complication empyema thoracis. However, the management of this complication still remains a taxing problem to the surgeon and internist. The treatments advocated vary from the extremes of aspiration alone to the use of wide thoracotomy. Regardless of the procedure used, the aim in the management of acute empyema is essentially the same; that is, to institute efficient drainage of the pleural cavity, to permit the lung to reexpand and to obliterate the free pleural space in order to prevent the development of chronic empyema.

The therapeutic value of penicillin in the treatment of cases of pneumococcic, streptococcic and staphylococcic infections has been well established. The most recent results obtained from its use have been summarized in the detailed report by Keefer and his associates.[1] The efficacy of penicillin in the management of empyema thoracis was mentioned in the work of Lyons,[2] who reported its use in 2 cases of nonbacteremic staphylococcic empyema with improvement. Dawson and Hobby [3] report the use of penicillin intrapleurally in 2 cases of pneumococcic empyema and in 1 case of staphylococcic empyema, with gratifying results. Tillett, Cambier and McCormack [4] reported the use of penicillin intrapleurally in 8 cases of pneumococcic empyema, in 7 of which the infection was controlled by local therapy without surgical drainage. Six of the patients recovered completely, while 1 patient insufficiently treated with penicillin had a recurrence of infection necessitating surgical drainage.

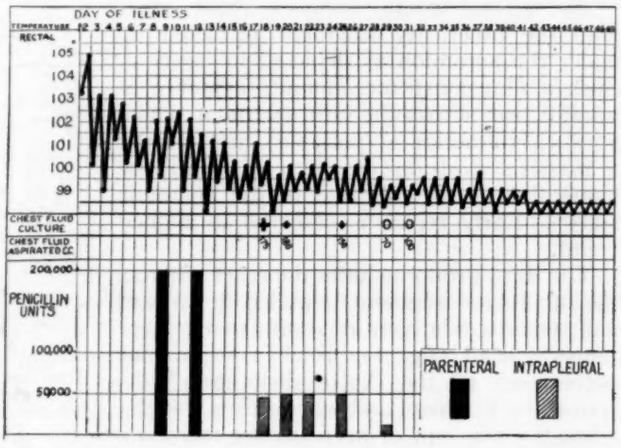

Fig. 1 (case 1).—Course in case of empyema secondary to bronchopneumonia, left lower lobe; nonhemolytic Staphylococcus aureus.

From the General Surgical and Communicable Diseases Sections, Tilton General Hospital, Fort Dix, New Jersey.

1. Keefer, C. S.; Blake, F. C.; Marshall, E. K.; Lockwood, J. S., and Wood, W. B.: Penicillin in the Treatment of Infections, J. A. M. A. **122**: 1217 (Aug. 28) 1943.
2. Lyons, C.: Penicillin Therapy of Surgical Infections in the United States Army, J. A. M. A. **123**: 1007 (Dec. 18) 1943.
3. Dawson, M. H., and Hobby, G. L.: The Clinical Use of Penicillin, J. A. M. A. **124**: 611 (March 4) 1944.
4. Tillett, W. S.; Cambier, M. J., and McCormack, J. E.: The Treatment of Lobar Pneumonia and Pneumococcal Empyema with Penicillin, Bull. New York Acad. Med. **20**: 142 (March) 1944.

This study comprises observations on 5 consecutive cases of empyema thoracis treated with intrapleural instillations of penicillin without surgical drainage. The etiologic agents varied considerably; in 2 cases the empyema was caused by nonhemolytic Staphylococcus aureus, 1 case by pneumococcus type III, 1 by a nonhemolytic streptococcus and 1 by a mixed infection containing a nonhemolytic streptococcus and hemolytic Staphylococcus aureus. In addition to the intrapleural instillation of the drug, parenteral penicillin was administered to patients who were felt to have underlying unresolved pneumonia, bacteremia or other complicating infections accessible to the blood stream.

Penicillin was supplied in the form of an amorphous powder in sealed ampules containing 100,000 units each. Solutions for parenteral or intrapleural use were prepared on the day of administration and kept constantly in the refrigerator at 5 C. For parenteral use the dry powder was dissolved in sterile saline solution so that 1 cc. contained 5,000 units. The individual dosage varied from 20,000 to 25,000 units administered every three hours by the intramuscular route. Solutions for intrapleural use contained 500 units per cubic centimeter and the usual intrapleural instillation contained 50,000 units dissolved in 100 cc. of sterile saline solution. Thoracentesis was accomplished under sterile precautions by entering the empyema cavity at the lowest possible level with a 15 or 17 gage needle. The pleural exudate was aspirated as completely as possible, sterile saline irrigations being used when necessary to thin out thick pus, which frequently obstructed the bore of the needle with fibrin plugs. Following aspiration, the penicillin solution was instilled into the pleural cavity. This procedure was repeated, usually on alternate days, and the frequency and duration of treatment depended on the response of the patient as manifested by fall of temperature, clinical appearance, bacteriology of the pleural exudate and the amount and rapidity of fluid reaccumulation.

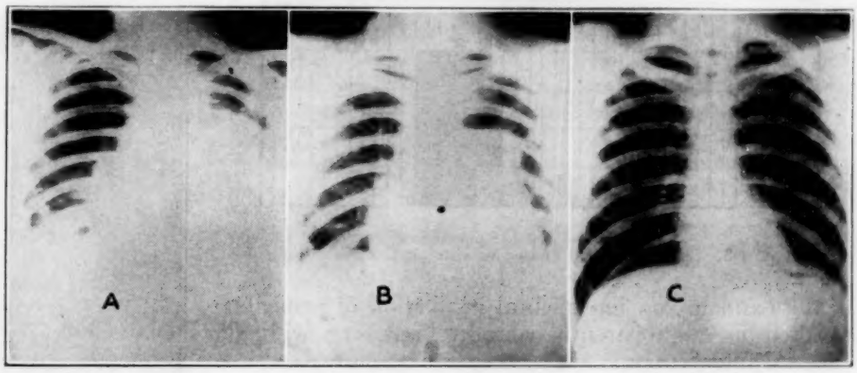

Fig. 2 (case 1).—*A*, 13th day of illness: a massive empyema on the left side with complete absence of aeration up to the second rib anteriorly. *B*, 18th day of illness: a large portion of the fluid has been aspirated; the remainder is loculated posteriorly. *C*, 92d day of illness: end result, normal chest.

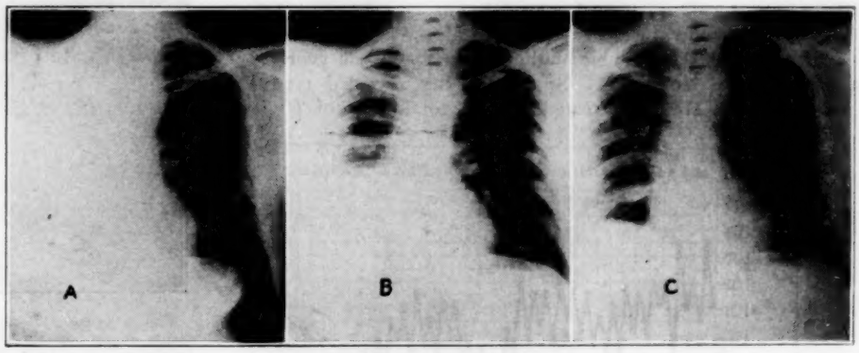

Fig. 3 (case 2).—*A*, 36th day of illness: a massive empyema on the right side, with total obliteration of pulmonary detail. *B*, 49th day: progress during therapy; much of the exudate has been aspirated; the fluid level is now at the 4th rib anteriorly. *C*, 59th day: the right diaphragmatic leaf is smooth in contour; minimal pleural thickening is noted in the region of the costophrenic sinus.

REPORT OF CASES

CASE 1.—A white man aged 23, diagnosed as having empyema secondary to bronchopneumonia, left lower lobe, nonhemolytic Staphylococcus aureus, was hospitalized on Dec. 4, 1943 because of pain in the left chest, fever, malaise, chills and cough productive of blood tinged sputum of one day's duration. Physical examination revealed signs of left lower lobe consolidation, which was confirmed by chest x-ray examination. Sulfadiazine therapy was instituted without therapeutic effect on the clinical course. The patient progressively developed dyspnea, orthopnea and cyanosis, and the temperature varied between 100 and 104.5 F., the pulse rate from 120 to 140 per minute and the respiratory rate from 30 to 40 per minute. Pneumococci could not be typed from the sputum, but many colonies of Staphylococcus aureus were present on culture. Sulfadiazine was discontinued on the ninth day of illness after a total dosage of 56 Gm. and penicillin therapy was started (fig. 1). On the ninth day of his illness he received 200,000 units of penicillin: 160,000 units intramuscularly (20,000 every three hours) and 40,000 units intravenously. The same dosage was repeated three days later, but the temperature continued to be septic and the patient appeared toxic and acutely ill. At this time a massive left pleural effusion was noted on x-ray examination (fig. 2 *A*).

The patient was transferred to the hospital for surgical drainage and came under our observation on the 17th day of his illness. At that time he was acutely ill, dyspneic, orthopneic and cyanotic, and clubbing of the fingers was demonstrable. His temperature was 101 F., and the white blood cell count was 12,300 with 76 per cent polymorphonuclear leukocytes. Examination revealed the presence of fluid throughout the entire left chest. Thoracentesis was performed and 175 cc. of thick, yellow, purulent exudate was aspirated and 45,000 units of penicillin dissolved in 90 cc. of sterile saline solution was instilled into the pleural space. Aspiration and instillations were repeated on the 20th, 25th, 29th and 31st days of illness, the amount of fluid removed varying from 70 to 180 cc. and the dosage of penicillin from 15,000 to 50,000 units. The pleural exudate revealed numerous colonies of nonhemolytic Staphylococcus aureus on culture. On subsequent aspiration the fluid became progressively thinner and cultures revealed diminishing numbers of bacterial colonies. Fluid aspirated on the 29th and 31st days of illness was thin, serous and sterile on culture.

The temperature declined by lysis and the patient's general condition progressively improved. He gained 35 pounds (16 Kg.) in weight and was discharged to duty three months after the completion of treatment. X-ray studies revealed progressive diminution in the size of the empyema cavity (fig. 2 *B*) and a chest plate taken three months after treatment revealed essentially normal lung fields (fig. 2 *C*). Diaphragmatic excursions were normal and there was no diminution of vital capacity.

At the onset the patient apparently developed a primary atypical pneumonia, which was complicated on or about the 13th day of illness by a Staphylococcus aureus empyema. This complication was not prevented by parenteral penicillin in the dosage given. Aspiration

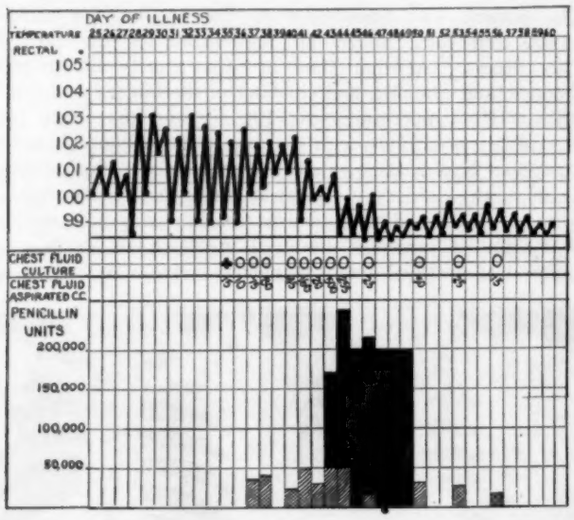

Fig. 4 (case 2).—Course in case of lobar pneumonia, empyema, pneumococcus type III. Penicillin: solid blocks, parenteral; shaded, intrapleural.

of the exudate and intrapleural instillation of penicillin resulted in an apparently complete recovery without surgical intervention.

Case 2.—A white man aged 32, diagnosed as having lobar pneumonia, empyema, pneumococcus type III, was hospitalized on Oct. 20, 1943 because of chills, fever, malaise and cough productive of sputum of one day's duration. Examination and a chest x-ray film showed consolidation of the right lower lobe. The temperature was 104 F. and the white blood cell count was 18,000 per cubic millimeter with 80 per cent polymorphonuclear leukocytes. Sputum typing revealed type III pneumococci. He was treated with a total dose of 60 Gm.

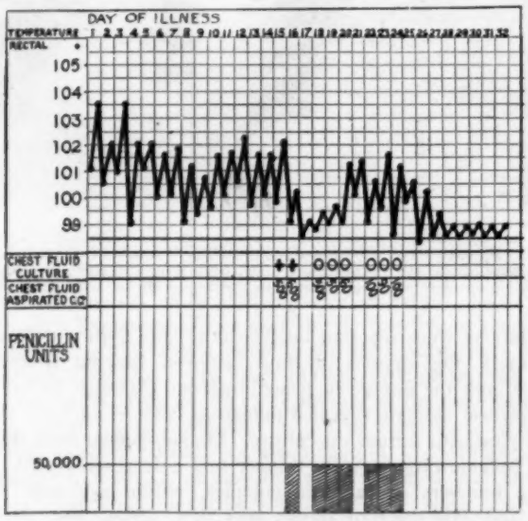

Fig. 5 (case 3).—Course in case of lobar pneumonia, empyema, mixed infection, pneumococcus type I, Staphylococcus aureus. Penicillin intrapleural.

of sulfadiazine over a period of twelve days. The temperature subsided by lysis and returned to normal after nineteen days. However, on the 22d day of illness the temperature began a gradual staircase rise and further examination revealed signs of fluid in the right chest. Thoracentesis on the 26th day yielded 500 cc. of thick, greenish exudate from which was cultured pneumococcus type III.

The patient came under our observation on the 34th day of his illness, at which time he was critically ill, cyanotic, dyspneic and orthopneic. There was clubbing of the fingers. The temperature was elevated to 103 F. and there were signs of a massive empyema of the right chest (fig. 3 *A*). Aspiration of the exudate and intrapleural penicillin instillations were instituted. Figure 4 indicates the plan of therapy and the clinical course of the patient. Thoracentesis was performed every one to two days for a period of two weeks, the amount of exudate varying from 15 to 500 cc. and the quantity of penicillin instilled from 15,000 to 50,000 units. The pleural fluid, which was at first thick, creamy and greenish, gradually became thin, clear and serous in consistency, and serial cultures were repeatedly sterile after the first instillation of 45,000 units of penicillin. Six days after the inception of local therapy the patient suddenly developed increased coughing and expectoration of mucopurulent sputum. As the temperature was still elevated, the patient was begun on parenteral penicillin,

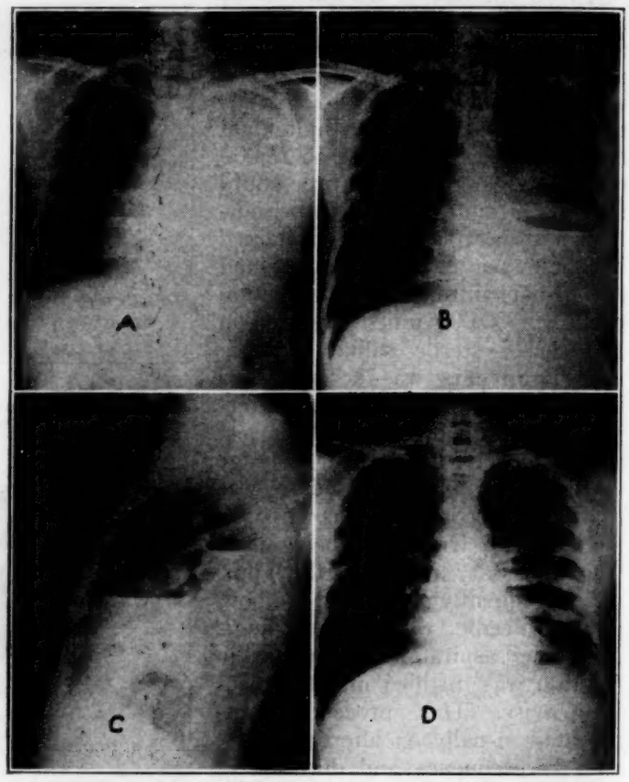

Fig. 6 (case 3).—*A*, 6th day of illness: a massive left empyema with displacement of the mediastinum to the right. *B* and *C*, 13th day: following aspiration of pleural exudate, two distinct fluid levels are present revealing anterior and posterior loculations; it was necessary to instil penicillin into each pocket. *D*, fifteen weeks after treatment: normal chest except for minimal pleural thickening.

25,000 units intramuscularly every three hours. The following day the patient coughed up 500 cc. of the same thick exudate; gas was aspirated from his chest cavity (fig. 3 *B*). Despite the development of the bronchopleural fistula, serial cultures of the pleural fluid remained sterile. Within two days the fistula closed spontaneously, as evidenced by cessation of the cough and expectoration. Penicillin was continued parenterally for three more days, but repeated aspiration and instillations of the drug were continued several days apart on four occasions to insure against reinfection. The patient made a rapid recovery, maintained a normal temperature and gained 45 pounds (20 Kg.) in weight. X-ray examination four months after the onset of illness showed the chest to be normal with the exception of slight pleural thickening in the region of the costophrenic sinus (fig. 3 *C*). Five months after illness the patient was on full active duty with no complaints.

A pneumococcus type III empyema complicated by a widely patent bronchopleural fistula recovered under parenteral and intrapleural penicillin therapy. The

pleural fluid remained sterile after the first instillation of 45,000 units of penicillin despite the presence of the fistula. Complete symptomatic recovery occurred within four weeks after the institution of penicillin therapy.

CASE 3.—A white man aged 37, diagnosed as having lobar pneumonia, empyema, mixed infection, pneumococcus type I, Staphylococcus aureus, was hospitalized on Feb. 18, 1944 with complaints of malaise, chills, fever and pain in the left chest. On admission he was acutely ill and the temperature was elevated to 102 F. Examination of the chest revealed the characteristic signs of a left lower lobar pneumonia. Chest x-ray films confirmed this diagnosis, and type I pneumococci were found in the sputum. The white blood cell count was 20,500 per cubic millimeter with 78 per cent polymorphonuclear leukocytes. He was treated with 74 Gm. of sulfadiazine over a period of twelve days without therapeutic response. He remained decidedly toxic and dyspneic and the temperature was septic, with intermittent elevations to 103 F. On the 6th day of illness he developed characteristic signs of a massive empyema of the left chest (fig. 6 *A*). Thoracenteses were done on the tenth and fifteenth days of illness, yielding on each occasion 500 cc. of thick, tenacious, creamy, greenish exudate, cultures of which revealed pneumococcus type I.

The patient came under our observation on the 16th day of his illness and was started immediately on aspiration and intrapleural penicillin therapy. At the time of the first treatment 660 cc. of thick, greenish fluid was aspirated and 50,000 units of penicillin instilled into the pleural cavity. Culture of the aspirated material revealed both type I pneumococcus and nonhemolytic Staphylococcus aureus. This and subsequent aspirations were difficult, owing to the thickness of the exudate, and irrigation with isotonic solution of sodium chloride was utilized to facilitate its evacuation. Figure 5 indicates the scheme of therapy followed and the clinical response of the patient. Ten aspirations in all were performed, yielding variously from 50 to 650 cc. of exudate. Instillations of penicillin were carried out on seven occasions, a total of 350,000 units.

Although the chest fluid was sterilized after the first instillation the patient remained acutely ill, toxic and febrile. The reason for the failure to respond promptly became apparent when subsequent chest films revealed two definite fluid levels, indicative of large fluid loculations anteriorly and posteriorly (fig. 6 *B* and *C*). Thoracenteses were now accomplished from each pleural pocket and penicillin instilled into each loculation on alternate days.

From this point on the temperature gradually subsided, the patient's general condition progressively improved and he remained afebrile. Fifteen weeks after therapy a chest x-ray taken prior to return to active duty showed a normal chest except for minimal pleural thickening (fig. 6 *D*). Fluoroscopy revealed normal diaphragmatic excursions.

A mixed type I pneumococcus and nonhemolytic Staphylococcus aureus empyema with loculations was treated with intermittent aspiration and instillation of a total of 350,000 units of penicillin intrapleurally without surgical intervention. The pleural fluid was sterilized after the first treatment with 50,000 units of the drug, but the temperature remained elevated until adequate evacuation of the exudate from both pleural loculations was accomplished.

CASE 4.—A white man aged 29, diagnosed as having empyema, nonhemolytic streptococcus, was hospitalized on Jan. 7, 1944 because of symptoms of cough, headache, malaise and sore throat of seven days' duration. On the day of admission he noted a chill and a stabbing pain in the left chest, which was aggravated on deep inspiration and coughing. The temperature was elevated to 105 F., respirations were labored and the mucous membranes were cyanotic. Physical examination and a chest x-ray film revealed evidence of consolidation of the left lower lobe. Cultures of the sputum revealed nonhemolytic streptococci. In addition to general supportive measures, which included parenteral fluid and oxygen, the patient was given 31 Gm. of sulfadiazine over a period of four days without beneficial response. It was now clinically apparent that the patient was suffering from a very virulent infection, and he continued critically ill, toxic, dyspneic and cyanotic. On the 10th day of illness he developed signs of a massive pleural effusion on the left side and a spread of the pneumonic process to the right, middle and lower lobes (fig. 7 *A*). Thoracentesis on the same day yielded 1,275 cc. of thin, blood tinged fluid which contained numerous nonhemolytic streptococci on smear and culture.

In view of the moribund condition of the patient and because of evidence of an underlying fulminating pneumonic process, sulfadiazine was discontinued and penicillin therapy was instituted both parenterally and intrapleurally. Figure 8 demonstrates the scheme of penicillin therapy and the clinical response of the patient. Eight thoracenteses were performed every one to three days during the ensuing thirteen days, the amounts removed varying from 60 to 550 cc. On each occasion 50,000 units of penicillin was instilled except on the second day of treatment, when 100,000 units was given. Over a period of fourteen days he received a total of 2,500,000 units of penicillin parenterally and 450,000 units intrapleurally. The pleural fluid, which had thickened during the first four days of the empyema, rapidly became thin and serous in consistency and remained sterile on culture following the first intrapleural instillation of penicillin. The temperature gradually subsided by lysis and his general condition progressively improved.

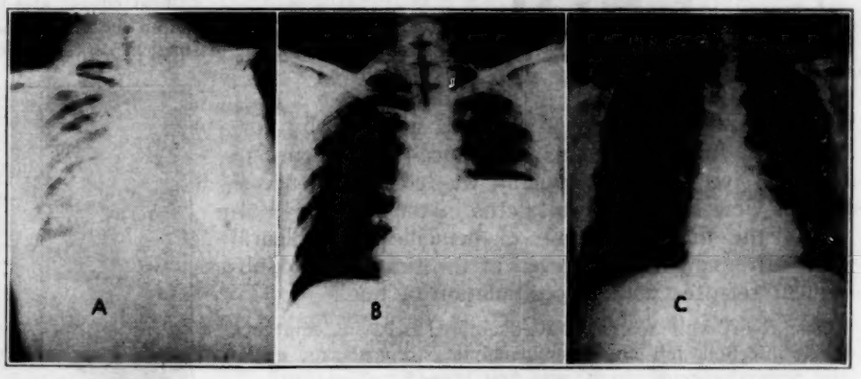

Fig. 7 (case 4).—*A*, 10th day of illness: a massive empyema on the left, with displacement of the heart and mediastinum to the right; a patchy type of consolidation involves almost the entire right lung. *B*, 34th day of illness: appearance of chest at the time of first relapse; there is a pyopneumothorax on the left with a fluid level at the 7th rib posteriorly; the heart and mediastinum are now in the midline and the right lung is clear. *C*, appearance of chest four months after onset of illness, showing a normal chest with the exception of slight pleural thickening in the left cardiophrenic angle.

On the 33d and 47th days of illness the patient had recrudescences of temperature elevation associated with reaccumulation of pleural fluid which remained sterile on culture (fig. 7 *B*). Three instillations of 50,000 units of penicillin were administered on alternate days during each of these relapses. On both occasions this treatment resulted in prompt subsidence of temperature and in clinical improvement of the patient.

Subsequently his temperature remained normal, he gained 29 pounds (13 Kg.) and he manifested no signs of decreased pulmonary function. The vital capacity was normal, there was no evidence of exertional dyspnea and the patient was returned to active duty five months after the onset of his illness. He was still on active duty and free of symptoms ten months after his illness. The final chest x-ray (fig. 7 *C*) revealed total reexpansion of the left lung and complete clearing of the

empyema with minimal residual thickening of the pleura in the cardiophrenic angle. Fluoroscopy revealed a normal range of diaphragmatic motion.

This critically ill patient with a nonhemolytic streptococcus pneumonia and empyema was treated with 2,500,000 units of penicillin parenterally and 750,000 units intrapleurally over a period of forty-one days.

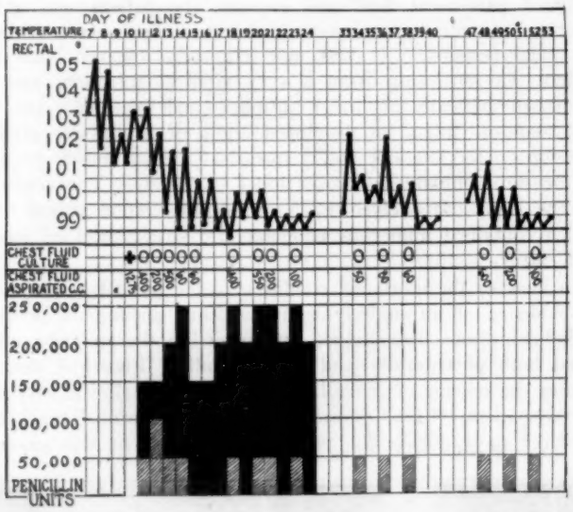

Fig. 8 (case 4).—Course in case of empyema, nonhemolytic streptococcus. Penicillin: solid blocks, parenteral; shaded, intrapleural.

He recovered completely, showing a substantially normal chest, functionally and anatomically. The use of such massive doses of penicillin was considered necessary in view of the critical status of the patient. Following the first instillation of penicillin, the pleural exudate remained sterile even at the time of two subsequent relapses with reaccumulation of fluid.

Case 5.—A white man aged 20, diagnosed as having empyema, mixed infection, left chest, nonhemolytic streptococcus, hemolytic Staphylococcus aureus, was first hospitalized on April 27, 1943 with a diagnosis of bronchopneumonia of the left lower lobe. The course was febrile, the white blood cell count varied from 18,000 to 30,000 per cubic millimeter and repeated sputum cultures revealed colonies of nonhemolytic streptococci. He was treated with a total of 52 Gm. of sulfadiazine over a period of seven days without therapeutic effect. Three weeks later he developed a massive pleural effusion (fig. 9 *A*). Thoracotomy was performed with the institution of closed intercostal drainage, which was unsuccessful in controlling the infection. Three weeks later resection of the eighth rib was performed and open tube drainage established. Temporary improvement followed, but despite persistent local treatment the pleural cavity could not be obliterated and the patient went on to develop an extensive chronic empyema. Drainage was profuse, cultures of the pus showing hemolytic Staphylococcus aureus and nonhemolytic streptococci.

The patient came under our observation six months after the onset of his illness. He was considerably underweight and showed intermittent temperature elevations to 101 F. A draining sinus tract was noted at the site of the previous thoracotomy. Instillation of iodized oil revealed a well demarcated, irregular, tubular empyema cavity 2.5 cm. in diameter (fig. 9 *B*). Culture of the purulent drainage from this tract revealed many colonies of hemolytic Staphylococcus aureus.

Local therapy was instituted, consisting of daily thorough aspiration of retained exudate by means of a small catheter and instillation of penicillin solution 250 units per cubic centimeter to the capacity of the pleural pocket. The total volume varied from 25 to 70 cc. over a period of eleven days, and the total amount of penicillin instilled was 104,600 units. Serial cultures of the aspirated exudate showed a progressive diminution in the total number of bacterial colonies until, near the completion of therapy, only an occasional colony was noted. In order to facilitate reexpansion of the lung and obliteration of the pleural space an occlusive dressing was applied to the sinus opening and an oxygen lavage of the pleural pocket was performed. The sinus tract gradually healed, and the patient became afebrile and symptomatically improved. Serial chest x-rays showed progressive, complete obliteration of the empyema cavity but a zone of thickened pleura remained (fig. 9 *C*).

Except for persistent anorexia and failure to gain weight adequately, the patient remained clinically improved, afebrile and ambulatory for four months following treatment. After that time he suddenly developed pronounced malaise, pain in the left chest and a sudden rise in temperature to 103 F. Examination and a chest x-ray film (fig. 9 *D*) revealed a large reaccumulation of fluid in the left pleural space. Aspiration yielded over 100 cc. of thick, greenish exudate, which showed hemolytic Staphylococcus aureus on culture. Fifty thousand units of penicillin was instilled on three occasions two days apart for a total of 150,000 units. The temperature subsided promptly after the second treatment and clinically the patient was much improved. The pleural exudate remained sterile on culture after the second instillation of penicillin.

Although control of the acute recurrence was obtained by the use of intrapleural penicillin, it was deemed advisable that open thoracoplasty be performed in view of the protracted clinical course and the presence of advanced structural changes within the chest. Accordingly he was transferred to a thoracic surgical center for consideration of such therapy.

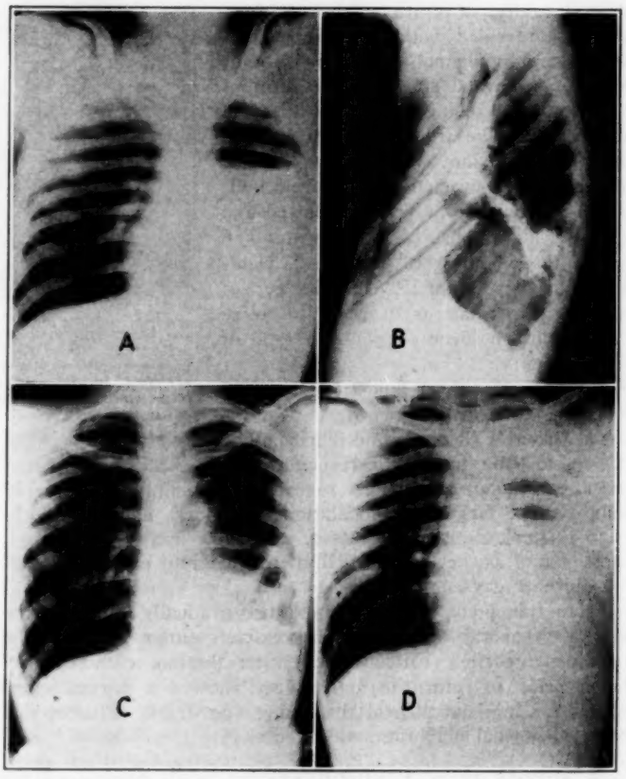

Fig. 9 (case 5).—*A*, 4th week of illness, showing pyopneumothorax on the left. *B*, end result five months after surgical drainage: iodized oil reveals a long tubular, pleural pocket extending from 3d rib posteriorly to the sinus opening in the 8th interspace. *C*, following penicillin therapy: chronic empyema cavity obliterated; a wide lateral zone of thickened pleura remains. *D*, four months after penicillin therapy: there is an extensive recurrence of fluid in the left lung.

This patient, with a mixed infection empyema containing a nonhemolytic streptococcus and a hemolytic Staphylococcus aureus, received apparently adequate surgical drainage but went on to develop an extensive chronic empyema. Intrapleural penicillin instillations resulted in closure of the pleural cavity and control of

the disease for a period of four months. At the end of this time there was an acute flare-up of the empyema, which again was controlled by intrapleural penicillin. The clinical course in this case would seem to indicate that, although a chronic empyema cavity may be sterilized and obliterated by local penicillin therapy, still recurrences of bacteriologically active infection may take place.

COMMENT

In observing the progress of these 5 cases, several points of importance in therapy became evident. It was considered important that treatment should be instituted at the earliest possible moment after the diagnosis of empyema had been established clinically and exudate obtained by aspiration. The organisms commonly causing empyema are susceptible to penicillin, and therapy need not await the bacteriologic identification of the etiologic agent.

Aspiration should be repeated at daily or two day intervals, depending on the amount and consistency of the exudate, the rate of reaccumulation of fluid and the clinical response of the patient. Thoracenteses should be performed at the lowest possible point in the empyema pocket, preferably under fluoroscopic control, using a large gage needle to facilitate aspiration. Irrigation with isotonic solution of sodium chloride was found to dilute thick, tenacious exudate and thus facilitate its aspiration. As much fluid as possible should be removed at each tapping, with the precaution that, in early cases with massive empyema, rapid removal of excessive amounts of fluid may result in mediastinal embarrassment. If a multilocular empyema exists, efforts must be made to aspirate each pocket thoroughly. Aspirations should continue until fluid does not reform. It has been observed, however, that small amounts of thin, sterile, serous fluid will be spontaneously absorbed by the patient within a short time.

Penicillin should be instilled after each aspiration at least until subsequent cultures of the fluid are proved to be sterile and the patient is clinically improved. The amount of the drug and the number of instillations necessary will vary with the clinical severity of the case and the type of organism involved. From 35,000 to 50,000 units was the dosage most frequently used and in our cases was found sufficient to effect sterilization of the exudate, even in the presence of a massive empyema.

With the therapy used the acute episode of empyema was controlled promptly in all 5 cases, as evidenced by fall in temperature, white blood cell count and sedimentation rate to normal levels, clinical improvement of the patient, rapid loss of exudate and reexpansion of the collapsed lung. In case 5 local treatment of an extensive chronic empyema resulted in arrest of the disease for four months, after which time an acute flare-up occurred. It is of interest that this secondary episode was also promptly controlled by intrapleural penicillin. However, because of the extensive underlying pleural thickening already present further radical surgery was deemed advisable to obtain obliteration of the chronic empyema cavity.

Following treatment, cases 2, 3 and 4 showed minimal pleural thickening, while the chest x-ray in case 1 was normal. In these 4 cases there was no deformity of the chest nor any diminution of the vital capacity. All showed normal diaphragmatic excursions on fluoroscopy. These patients have been followed for from three to ten months after treatment and all have returned to active military duty.

SUMMARY

Five patients with empyema of varying etiology were treated with aspiration and intrapleural instillation of penicillin. Four patients with acute empyema recovered with little or no pleural thickening and were returned to military duty within three to five months after the onset of illness. One patient with chronic empyema with an acute exacerbation responded to therapy in the acute phase of the disease but eventually required further surgery.

THE MEDICAL TREATMENT OF ACUTE EMPYEMA

REPORT OF FIVE CASES CURED WITH CHEMOTHERAPY AND THORACENTESES

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The addition of sulfonamides and penicillin to our therapeutic armamentarium has changed radically the treatment of many infectious diseases. Treatment of empyema with the newer agents was tried with varying results. According to most authorities, empyema is a disease usually requiring open or continuous closed drainage. Early thoracotomy is recommended in pneumococcic empyemas. Repeated aspirations are ordinarily performed in postpneumonic streptococcic empyemas until the underlying inflammatory process subsides and the purulent exudate becomes thickened, when thoracotomy with rib resection is performed.

The mortality of empyema varies with the etiology, the virulence of the infecting organisms and the resistance of the patient. Moschcowitz's [1] mortality figures for empyema in patients of all ages vary between 18.9 per cent and 45 per cent and he quotes Graham's figure for average mortality in army camps from empyema as 30.2 per cent. It is well known that in anaerobic infections following lung abscesses prognosis is poor. Eloesser [2] writes "Most fatal is the empyema caused by sudden rupture of a lung abscess into a defenseless virgin pleural cavity," and he compares anaerobic empyemas to the fulminating diffuse peritonitis following a ruptured bowel.

Review of the literature by Bufford and Blades [3] shows a reduction in the incidence of empyema following pneumonia from 5 per cent to 1 per cent since the introduction of sulfonamide therapy. However, when empyema does occur after the use of the sulfonamide drugs such cases are more difficult to treat. In their series of 30 cases of unselected empyemas, which occurred during or after sulfonamide treated pneumonias, two deaths occurred, in 2 cases it was necessary to perform secondary drainage operations and in 9 cases there was considerable delay in the expansion of the lung.

The poor results of the treatment of empyema reported in the literature have led to search for other methods of therapy of this serious complication. Keefer,

1. Moschcowitz, cited by Irons, E. E.: Empyema, in Cecil, R. L.: Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1942, p. 983.
2. Eloesser, L.: Acute Empyema, in Christopher, F.: Textbook of Surgery, Philadelphia, W. B. Saunders Company, 1942, pp. 959-964.
3. Bufford, T. H., and Blades, B.: The Influence of Sulfonamide Therapy on Post-Pneumonic Empyema, J. A. M. A. **118**: 950-952 (March 21) 1942.

Blake and their associates [4] were among the first to report the use of penicillin in empyema. We feel that it may be of interest to report 5 consecutive cases of acute empyema of varied etiology, 2 of which followed rupture of lung abscesses into the pleural cavity, treated medically in a somewhat unorthodox manner.

REPORT OF CASES

CASE 1.—A white man aged 26 was admitted Dec. 13, 1943 to the hospital because of a sulfonamide resistant acute gonorrhea complicated by a right epididymitis. On December 20, one week after admission, the patient developed a severe lancinating pain in the right side of his chest, aggravated by deep inspiration and cough. His temperature was 99 F. orally; breath sounds were found to be diminished over the right base and no rales were heard. The patient improved subjectively during the next few days, but on December 23 he became much worse and appeared acutely ill; his temperature rose to 105 F. Signs of diffuse pneumonic involvement in the right lung were confirmed by x-ray examination of the chest, which showed a diffuse stringy infiltration throughout the right lung field. The white blood cell count on December 23 was 13,500, with 92 per cent polymorphonuclears. Sulfadiazine therapy was started the same day. The patient became cyanotic and was placed in an oxygen tent. He expectorated 3 to 4 ounces of bloody sputum daily, and his temperature fluctuated between 101 and 105 F. orally. An x-ray of the chest taken on December 27 showed a "hydropneumothorax," right side, with a fluid level reaching up to the seventh rib posteriorly, which was ascribed to a bronchopleural fistula. Blood culture was negative. The sputum showed hemolytic Streptococcus alpha on smear and culture. The patient's general condition became progressively worse in spite of sulfadiazine therapy, and he appeared to be critically ill. Seventy-four Gm. of sulfadiazine and 8 Gm. of sulfanilamide had been given orally with no apparent effect on the patient's condition.

On Jan. 5, 1944 penicillin therapy was started. On that day the red blood cell count was 3,790,000, with 80 per cent hemoglobin. The white blood cell count was 24,250, with 90 per cent polymorphonuclears and 10 per cent lymphocytes; the sedimentation rate was 52 mm. per hour. Twenty-five thousand units of penicillin was given intramuscularly every three hours. In addition, a thoracentesis was done and 350 cc. of hemorrhagic pus was removed from the right side of the chest and replaced by 100,000 units of penicillin in isotonic solution of sodium chloride. The chest fluid showed many pus cells and red blood cells with diffuse hemolysis, but no bacteria were found on smear or culture. The patient felt somewhat better the next day and his expectoration diminished. Thoracentesis was repeated January 7 and 250 cc. of reddish brown pus was removed from the right side of the thorax and replaced by 100,000 units of penicillin in 125 cc. of saline solution. Transfusion of 500 cc. of blood was given the same day because of the patient's anemia. The temperature became normal January 9 and remained normal, while leukocyte and differential counts were reported to be within normal limits. Aspiration of the right side of the chest was again performed January 13, and it was noted that the exudate changed from reddish brown to green; 210 cc. of pus was withdrawn and replaced by 50,000 units of penicillin in 100 cc. of saline solution. The patient improved and a definite decrease in the amount of sputum, with a loss of its bloody character, was noted.

On January 12 the intramuscular penicillin was decreased to 90,000 units daily and was discontinued altogether on January 17. A total of 1,850,000 units of penicillin had been administered to the patient, of which 250,000 units had been injected locally into the pleural cavity. The final thoracentesis was performed on January 21, when 50 cc. of greenish pus was removed from the chest, with no replacement by penicillin. The patient felt well; dulness on percussion at the right base with diminished breath sounds persisted. X-ray of the chest on January 29 showed increased density at the right base with no fluid level seen. A gradual clearing of the density of the right lung, ascribed to resolving fibrinous pleurisy, was noted on serial x-rays. The sedimentation rate dropped to 10 mm. per hour on February 10. The patient became ambulant early in February; he was given a convalescent furlough March 10 and was discharged to duty two and one-half months later.

CASE 2.—A white man aged 21, a German prisoner of war, gave a history of having been shot on May 4, 1943, with a shell fragment entering the left side of his chest at about the sixth rib posteriorly and leaving the left axilla in the region of the eighth rib. He was treated in a hospital in North Africa for about three months and was sent to the United States about Nov. 8, 1943.

He felt well and had no complaints until Jan. 14, 1944, when he began to have chills, fever, fatigue, weakness and pains in the left side of the chest on deep inspiration. No history of cough, sore throat or dyspnea was elicited.

He was admitted the following day to the station hospital, where on examination his oral temperature was 102 F., pulse rate 96 and respiratory rate 22. Dulness on percussion with suppression of breath sounds in the left lung, more prominent over the left base, was found. No rales were heard and no cyanosis was noted. The blood count on January 16 showed that white cells were 14,650, with 77 per cent polymorphonuclears and 21 per cent lymphocytes. The patient was given sulfadiazine therapy and his temperature subsided in a few days. He became ambulant but had a relapse January 28 with pain in the left side of the chest and rise of temperature to 104 F. X-rays of the chest taken January 17 and January 28 revealed "hydropneumothorax," left side, with fluid about the level of the fourth rib anteriorly and displacement of the heart to the right. Thickening of the pleura along the lateral chest wall was noted, with irregular defects in the left sixth and seventh ribs. Thoracentesis was performed and 30 cc. of thick, foul pus was removed from the left side of the chest. Aspiration of the chest was repeated January 30 and 300 cc. of purulent fluid was withdrawn. Culture of the pleural fluid showed gram positive cocci. The patient was transferred February 6 to this hospital for observation and treatment.

On examination in this hospital the patient appeared to be toxic and emaciated. The temperature fluctuated between 97 and 104.6 F. On physical examination signs of fluid over the right base were found and were confirmed by x-ray examination of the chest. It was felt that the patient had a pyopneumothorax secondary to osteomyelitis of the sixth and seventh ribs. A thoracentesis was performed February 8. One hundred and fifty cc. of thick, greenish, foul pus was withdrawn from the left side of the chest posteriorly and the pleural cavity was irrigated with 1:3,500 of fresh aqueous azochloramid. Sulfadiazine was given at the same time orally. Culture of the pleural fluid showed Proteus vulgaris and Staphylococcus aureus. On February 9 the white blood cells numbered 15,650, with 69 per cent polymorphonuclears and 30 per cent lymphocytes, and the sedimentation rate was 49 mm. per hour. Thoracenteses and irrigations of the pleural cavity with fresh 1:3,500 azochloramid aqueous solution were repeated approximately every other day. From 300 to 400 cc. of pus was removed each time and from 120 to 150 cc. of azochloramid solution was injected into the pleural cavity after each irrigation. The sulfadiazine level was about 9 mg. per hundred cubic centimeters. On this treatment the pus became progressively more fluid and less foul. As the patient's condition improved, aspirations were done less frequently and, on February 24, 100 cc. of clear serous fluid was removed from the left side of the chest and no irrigation with aqueous azochloramid was performed. The fluid gradually absorbed, and on the last x-ray, taken March 9, no fluid in the chest was seen and the left lung was reexpanding. The temperature became normal on February 17 and the patient remained afebrile during his stay in the hospital. A total of 45 Gm. of sulfadiazine was given to the patient. The blood count gradually subsided to normal, and the last sedimentation rate was 10 mm.

4. Keefer, C. S.; Blake, F. G.; Lockwood, J. S., and Wood, W. B.: Penicillin in the Treatment of Infections, J. A. M. A. **122**: 1217-1224 (Aug. 28) 1943.

per hour. The patient had no subjective complaints during his last three weeks of hospitalization, was ambulant, and was transferred to another general hospital for administrative reasons March 15, 1944.

CASE 3.—A white man aged 25, a German war prisoner, was admitted to the station hospital Oct. 17, 1943 with a history of pain in the chest and dyspnea of twenty-four hours' duration; his temperature on admission was 104 F. Physical examination revealed irregular dulness and flatness, bronchial breathing and fine crepitant rales throughout both lower lobes posteriorly. A diagnosis of lobar pneumonia, both lower lobes, was made; x-rays of the chest showed at first a pneumonic process in the left lower lobe, with later spread of pneumonic involvement to the right lower lobe. Sulfadiazine therapy was started October 17 and discontinued October 28, with a total of 84.5 Gm. given. Oxygen therapy was administered at the same time. Sputum examinations showed Staphylococcus aureus, Staphylococcus albus and Friedländer's bacilli on various occasions. The white blood cell count varied from 6,300 to 12,250. The sulfadiazine level fluctuated between 10.8 and 17.8 Gm.

In spite of the intensive sulfadiazine therapy the patient's temperature remained elevated, fluctuating between 98.2 and 103 F. It subsided about October 27, only to rise again to 104 F. two days later, and then fever continued up to 101.4 F. Signs of fluid in the left base were elicited. On serial x-ray films an area of increased density suggestive of pneumonic involvement in the right pericardiac region was noted; in the left lung field a sharply circumscribed mass, radiating from the hilar area and extending about half way to the chest wall, suggestive of encapsulated empyema, was seen. Culture of the sputum was positive for hemolytic Staphylococcus aureus. On Jan. 4, 1944 a thoracentesis was done and 20 cc. of thick pus was withdrawn from the left side of the chest. Staphylococcus albus was isolated on smear and culture from the chest fluid. The patient was transferred January 12 to this hospital for treatment.

On admission to this hospital the patient appeared to be toxic and weak. He had a severe cough and a low grade fever with occasional rise to 102 F.; on physical examination signs of fluid at the left base were elicited. A thoracentesis was done and 400 cc. of sanguineous, purulent fluid was removed from the left side of the chest and 50,000 units of penicillin in 200 cc. of saline solution was injected into the empyema cavity. Smear and culture of the fluid showed Staphylococcus aureus. An x-ray film of chest taken the next day showed an increase in density in the left side, with apparent rupture of the encapsulated empyema into the pleural cavity. The blood count was essentially normal. On January 19 a second thoracentesis was done and 175 cc. of hemorrhagic purulent fluid was removed and replaced by 32,500 units of penicillin in 130 cc. of saline solution. Staphylococcus albus was isolated from this fluid on smear and culture. On January 28 a third thoracentesis was done and 100 cc. of pus was withdrawn and 25,000 units of penicillin in 100 cc. of saline solution was injected into the empyema cavity. The fluid withdrawn proved to be sterile on smear and culture. An x-ray film of the chest on January 26 showed an area of increased density to be smaller, with a small localized pyopneumothorax near the left side of the mediastinum, with fluid level at the anterior end of the third left rib. The patient's temperature dropped to normal January 28 and remained normal. On February 15 x-ray examination of the chest showed only slight thickening of the pleura in the left mediastinal region. The localized area of density and fluid level had apparently disappeared; obliteration of the left costophrenic sinus was noted; the right lung was apparently clear. The patient improved subjectively and had very few complaints except for occasional pains in the left side of chest. A total of 107,500 units of penicillin had been injected into the pleural cavity during the three thoracenteses. No other specific therapy was given during his stay at this hospital. The patient was discharged from the hospital for administrative reasons in the beginning of March 1944.

CASE 4.—A white man aged 25 was admitted to the station hospital Feb. 21, 1944 because of an upper respiratory infection, which was followed by a diffuse pemphiginous eruption consisting of vesicles and bullae, varying in size up to half a dollar (30 mm.) and involving the mucosa of the oral cavity and conjunctiva; the eruption rapidly spread and covered most of the body. The temperature fluctuated between 99 and 106 F. The patient was treated with 440,000 units of penicillin administered between February 27 and March 5. By March 11 the bullae disappeared with resultant macular stains and persistent fetor oris. On March 13 the patient began to complain of pain in the lower right side of the chest; his temperature rose to 103 F. Breath sounds were diminished over the right base and x-ray examination of the chest showed pneumonic involvement in the right lower lobe. Penicillin therapy was started again; 5,000 units was administered intramuscularly every two hours and discontinued on March 16. A total of 150,000 units was given in three days. A diagnosis of lung abscess, right side, confirmed by x-ray examination of the chest, was made on March 20. Rapid progressive increase in the abscess was noted, and penicillin therapy was renewed March 21 with about 120,000 units given by March 23, at which time it was discontinued. The patient was expectorating about 1 pint of foul, bloody mucopus daily. He became rapidly worse, he had chills and his temperature was fluctuating between 98 and 105.6 F. orally. A total of about 710,000 units of penicillin was given during the three periods of treatment in the station hospital. Because of a progression of the pathologic condition the patient was transferred to this hospital on March 30, 1944.

On admission to this hospital the patient appeared to be toxic, somewhat irrational and critically ill; his temperature was 104.4 F. On physical examination signs of fluid over the right base and of acute diffuse bronchitis were elicited. The white blood cells numbered 24,000, with 80 per cent polymorphonuclears; the sedimentation rate was 62 mm. per hour; blood culture was negative. X-ray examination of the chest showed diffuse irregular density throughout the middle and lower lobes of the right lung; density in the right base was noted, with a shifting fluid level in the seventh interspace posteriorly, reaching the chest wall laterally. The impression from clinical and x-ray findings was lung abscess, with rupture into the pleural cavity and resulting empyema at the right base.

The patient was placed in an oxygen tent and on postural drainage. Sulfadiazine therapy was started on admission, supplemented April 1 by 25,000 units of penicillin intramuscularly every three hours because of his presumably mixed infection. He expectorated about 6 ounces of bloody, greenish sputum daily, at times foul in character. Sputum examination showed alpha streptococci, Staphylococcus aureus and Neisseria catarrhalis.

A thoracentesis was performed April 2, and 250 cc. of sanguineous, foul pus was removed and replaced by 50,000 units of penicillin in isotonic solution of sodium chloride. Laboratory examination of the purulent exudate showed nonhemolytic streptococci on culture; the pleural fluid sugar was too low to be determined colorimetrically; the white blood cells numbered 33,000, with 86 per cent polymorphonuclears and diffuse hemolysis of red blood cells. Thoracentesis was repeated two days later and 210 cc. of greenish pus was removed from the right pleural cavity. The pleural fluid was not as foul as it was the first time, and it was negative on smear and culture for pathogenic micro-organisms, as were succeeding pleural fluids; 100,000 units of penicillin in 100 cc. of isotonic solution of sodium chloride was injected into the pleural cavity. A transfusion of 500 cc. of blood was given the same day because the patient's hemoglobin had dropped to 52 per cent. The patient continued to improve and his temperature subsided to 99-101 F. Thoracentesis was repeated April 6, with 70 cc. of greenish pus removed and replaced by 200,000 units of penicillin intrapleurally. His temperature subsided to normal April 7 and remained normal. The expectoration decreased gradually to 1 to 2 ounces daily and became greenish instead of bloody and lost its foul odor. On April 7 the red blood cells numbered 3,520,000, hemoglobin 78 per cent Sahli, white

blood cells 7,600, with essentially normal differential count. Another thoracentesis was performed April 10 and 70 cc. of greenish pus was removed and replaced by 40,000 units of penicillin in isotonic solution of sodium chloride; the same day the penicillin dosage was cut to 90,000 units intramuscularly and sulfadiazine was diminished to 4 Gm. daily. The blood sulfadiazine level fluctuated between 5.3 and 8 mg. per hundred cubic centimeters. The patient continued to improve; cough and expectoration disappeared and his appetite was good.

On April 17 the last thoracentesis was performed and 20 cc. of yellowish brown seropurulent fluid was removed from a small empyema pocket between the eighth and ninth ribs posteriorly. The cavity was irrigated with saline solution and 8,000 units of penicillin was instilled intrapleurally. Sulfadiazine therapy was discontinued April 14, while penicillin was discontinued April 17. A total of 78 Gm. of sulfadiazine was administered; 2,445,000 units of penicillin was given to the patient intramuscularly and 398,000 units into the pleural cavity. The patient improved steadily; he gained about 35 pounds (16 Kg.) during his stay in the hospital. Serial x-ray films of the chest showed thickening of the right pleura and obliteration of the right costophrenic sinus, with progressive resolution in the pleural pathologic condition. The last x-ray examination of the chest showed elevation of the right diaphragm, but the right lower lobe appeared to be clear otherwise. The patient became ambulatory about April 25. He became progressively more active but because of a residual persistent bronchitis was discharged from the Army the beginning of August 1944.

Case 5.—A white man aged 30 gave a history of chronic cough for about three years. He had had malaria in September 1942, with recurrence in June 1943. About March 28, 1944 he began to have severe pain in the left side of his chest, aggravated by deep inspiration; he was admitted to the station hospital April 3, 1944.

On admission his temperature was 101.4 F. orally. Physical examination of the chest revealed pneumonic involvement of the left lower lobe. The white blood cells numbered 14,100, with 84 per cent polymorphonuclears. The sedimentation rate was 55 mm. per hour. The sputum was negative for pneumococci and tubercle bacilli. The x-ray film of the chest taken April 4 showed an elliptic area of decreased density suggestive of cavity formation with fluid level, probably lung abscess, in the left lung field. The patient was placed in an oxygen tent, and sulfadiazine was given for three days, with the blood level reaching 10.2 mg. per hundred cubic centimeters. As the patient did not improve, sulfadiazine therapy was replaced by penicillin April 6; 25,000 units was given intramuscularly every three hours. An x-ray film of the chest taken April 8 showed an increase in pneumonic involvement and two areas of increased density suggestive of a double lung abscess on the left side. A thoracentesis was attempted, but no fluid was obtained. Because of rapid progression of the pulmonary lesions in spite of intensive therapy, the patient was transferred to this hospital April 8 for further treatment and observation.

On admission to this hospital the patient appeared to be seriously sick. His face was flushed and he reacted sluggishly. His temperature was 102 F. on admission and fluctuated between 98.4 and 103 F. rectally; the pulse rate was 120. Signs of fluid in the left base up to about the seventh rib posteriorly and some crepitant rales above that area were noted; many sibilant rales were heard throughout the right side of the chest. The red blood cells numbered 4,090,000, with hemoglobin 76 per cent Sahli and white blood cells 17,550, with 83 per cent polymorphonuclears. Smear and culture of the sputum showed Staphylococcus aureus and alpha streptococci; blood culture was negative. X-ray examination of the chest showed diffuse density in the left base, with a definite fluid level extending to the left axilla in the region of the seventh rib. Because of clinical and x-ray findings, it was felt that the patient had a double lung abscess which had fused and ruptured into the pleural cavity with formation of an empyema.

Because of the severity of the disease and probable mixed infection, the patient was treated with a combination of sulfadiazine and penicillin. Sulfadiazine 4 Gm. followed by 1 Gm. every four hours, with an equal amount of sodium bicarbonate, was administered orally; 25,000 units of penicillin was given intramuscularly every three hours. The patient was placed on postural drainage and he expectorated from 5 to 6 ounces of yellowish green sputum daily. A thoracentesis was performed April 10 and 75 cc. of greenish foul pus was removed from the left pleural cavity and replaced by 60,000 units of penicillin in isotonic solution of sodium chloride. Smear and culture of the pleural fluid showed gram positive cocci in chains, gram positive rods and gram negative rods. On April 12 another thoracentesis was done and 250 cc. of greenish yellow pus was removed from the left side of the chest and replaced by 100,000 units of penicillin in isotonic solution of sodium chloride.

Thoracenteses were repeated about every other day, with removal of greenish yellow pus varying in amount from 320 cc., April 17, to 70 cc. on April 26. The purulent fluid was replaced by 50,000 to 100,000 units of penicillin each time. Pus became gradually less foul until it lost its odor completely; cultures and smears of pleural fluids were persistently negative for pathogenic micro-organisms following the first positive smear and culture of pleural fluid. On April 17 416,000 white blood cells per cubic millimeter were reported on examination of the chest fluid, with 92 per cent polymorphonuclears and 8 per cent lymphocytes. Blood cell and differential count showed a mild leukocytosis with hemoglobin 94 per cent Sahli. The blood sulfadiazine level varied between 3.9 and 10.2 mg. per hundred cubic centimeters. Blood and stool cultures were negative for parasites. On May 6 the last thoracentesis was performed and 30 cc. of yellowish green purulent odorless fluid was withdrawn from the pleural cavity and replaced by 10,000 units of penicillin in saline solution. The sedimentation rate was reported as 46 mm. per hour on April 25, 23 mm. per hour on May 8, 7 mm. per hour on May 24 and 4 mm. per hour on July 8.

A total of 79 Gm. of sulfadiazine was given orally between April 8 and April 22; 2,450,000 units of penicillin was given intramuscularly and 560,000 units was injected into the pleural cavity. Serial x-rays of the chest showed progressive diminution in pleural pathologic change in the left side of the chest, and the last x-ray of the chest, taken July 8, showed a slight residual fibrosis throughout the left lower lobe, with elevation of the left diaphragm and partial obliteration of the left costophrenic sinus.

The patient has been feeling well, although he has had a cough; on examination, some sibilant and sonorous rales were heard throughout the chest, ascribed to an underlying allergic bronchitis. He was given a convalescent furlough June 26 and was sent for rehabilitation July 13. The general condition of the patient is good at the time of this report.

COMMENT

Five unselected patients with acute empyema, all seriously sick when first seen, were treated medically. Three of the cases were putrid empyemas, 2 of which followed ruptured lung abscesses with bronchopleural fistulas. We were impressed by the severity of the infection as shown by the hemorrhagic type of the purulent exudate in 4 of the cases, and the anaerobic type of infection in cases 2, 4 and 5, as evidenced by the foul odor of the pus. Lyons [5] has reported 4 cases of lung abscess, 2 of which were putrid and were not benefited by penicillin therapy, and 2 pyogenic cases in which improvement occurred after treatment with penicillin; 1 patient with hemolytic streptococcic empyema died in spite of treatment with penicillin. We feel that the cures in our 2 cases of lung abscess were probably due to the rupture into the pleural cavity, where the infection was more accessible to the effect of the therapeutic agents used.

5. Lyons, C.: Penicillin Therapy of Surgical Infections in the United States Army, J. A. M. A. **123**: 1007-1018 (Dec. 18) 1943.

Keefer, Blake and their associates [4] reported 5 cases of postpneumonic empyemas, 2 of which improved after penicillin treatment; in 7 of 9 of their cases of staphylococcic empyema improvement or recovery followed treatment with the same therapeutic agent. Two of 3 cases of lung abscesses were treated by the same authors with penicillin; they reported two cures and one death, in spite of treatment.

In putrid empyemas repeated thoracenteses are considered definitely contraindicated by some writers. Maier and Grace [6] felt that aspiration in such cases was associated with considerable danger of infection of the chest wall. Four of their patients developed phlegmonous infections of the thoracic wall, and 2 of their patients, who were subjected to aspiration twice before thoracotomy, died. These authors concluded, therefore, that open thoracotomy with rib resection was the procedure of choice as soon as the diagnosis of putrid empyema was confirmed by diagnostic aspiration.

In our experience, a combination of sulfadiazine and penicillin given at the same time and associated with repeated aspirations of purulent exudate and its replacement by penicillin proved to be beneficial in cases of mixed infections, aerobic or anaerobic. No untoward effects were noted in putrid empyemas from repeated thoracenteses. We fully agree with Keefer, Blake and their associates that it is impossible at present to sterilize empyema cavities by the parenteral use of penicillin alone. Neither penicillin nor sulfadiazine, nor the combination of the two, can take the place of good medical judgment in replacing accumulations of pus with penicillin or azochloramid.

We were favorably impressed with the effect of combined sulfadiazine and azochloramid therapy in case 2, from the pleural fluid in which Proteus vulgaris and Staphylococcus aureus were isolated. It may be well worth further trial in cases not responding to penicillin therapy.

The importance of chemotherapy and antibiotics in treatment of infectious diseases is increasing steadily. We fully appreciate that the series of empyemas presented is too small to serve as the basis for definite conclusions, but the results are so encouraging that further trial with medical treatment of empyema as outlined is fully justified. The treatment of empyema, however, continues to be both a medical and a surgical problem.

SUMMARY

1. Two cases of putrid empyema due to ruptured lung abscesses were treated with combination of sulfadiazine and penicillin. Penicillin was administered intramuscularly and intrapleurally following repeated thoracenteses. Treatment resulted in rapid improvement and cure.

2. One case of postpneumonic empyema was treated with penicillin intramuscularly and intrapleurally, following repeated thoracenteses, with rapid improvement.

3. One case of postpneumonic empyema, apparently caused by Staphylococcus aureus and Staphylococcus albus, was treated with penicillin locally, following aspirations of pus, with progressive improvement and cure.

4. One case of empyema, apparently caused by Staphylococcus aureus and Proteus vulgaris, was treated with sulfadiazine orally, repeated thoracenteses and azochloramid intrapleurally, with rapid cure.

6. Maier, H. C., and Grace, E. J.: Putrid Empyema, Surg., Gynec. & Obst. **74**: 69-74 (Jan.) 1942.

ADDENDUM

Since completion of this paper, one of us (H. R.) has successfully treated medically 3 more cases of empyema. Sulfadiazine orally and azochloramid instilled locally following each of repeated thoracenteses were used in 1 case. In 2 others, 1 complicating staphylococcic septicemia, local and parenteral penicillin was employed in addition to oral sulfadiazine and repeated aspirations of empyema cavities.

THE VALUE OF PENICILLIN IN THE TREATMENT OF EMPYEMA

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DETROIT

Penicillin is almost nontoxic for man, yet it exerts a powerful antibacterial action against a wide variety of micro-organisms. Unlike the sulfonamides, penicillin is not inhibited by pus or other products of tissue destruction.[1] When given intravenously or intramuscularly, it penetrates poorly into collections of pus, but if it is injected directly into an abscess it remains there for some time and may be found in considerable concentration as long as twenty-four to forty-eight hours after its injection.[2] These unusual properties of penicillin have led some workers [3] to treat empyema by aspiration of the pus, followed by instillation of penicillin. Theoretically, if this form of treatment is to be successful, the following conditions should prevail:

1. The causative bacteria must be susceptible to penicillin.

2. It must be possible for penicillin instilled in the empyema to contact all of the bacteria. Some empyemas are loculated so that it is impossible to reach all of the pockets with an aspirating needle.

3. The cavity must not contain pieces of necrotic lung or large clots of fibrin. Many empyemas of long standing, especially those caused by pneumococci, contain clots of fibrin several inches in diameter. An occasional empyema contains a piece of necrotic lung in the interstices of which bacteria are protected. Penicillin will not sterilize an empyema until these fibrin clots and pieces of necrotic lung are removed.

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2. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**: 425-437 (May) 1943.

3. Bennett, T. I., and Parkes, T.: Penicillin in Sulfonamide Resistant Pneumonias with Special Reference to Staphylococcal Infection and Empyema, Lancet **1**: 305-308 (March 4) 1944. Bloomfield, A. L.; Kirby, William, and Armstrong, C. D.: A Study of "Penicillin Failures," J. A. M. A. **126**: 685-691 (Nov. 11) 1944. Butler, E. C. B.; Perry, K. M. A., and Valentine, F. C. O.: Treatment of Acute Empyema with Penicillin, Brit. M. J. **2**: 171-175 (Aug. 5) 1944. D'Abreu, A. L.; Litchfield, J. W., and Thomson, Scott: Penicillin in the Treatment of War Wounds of the Chest, Brit. J. Surg. (supp.) **32**: 179-198 (July) 1944. Dawson, M. H., and Hobby, G. L.: The Clinical Use of Penicillin: Observations in 100 Cases, J. A. M. A. **124**: 611-622 (March 4) 1944. Jeffrey, J. S., and Thomson, Scott: Penicillin in Battle Casualties, Brit. M. J. **2**: 1-4 (July 1) 1944. Keefer, C. S.; Blake, F. G.; Marshall, E. K.; Lockwood, J. S., and Wood, W. B.: Penicillin in the Treatment of Infections: A Report of 500 Cases, J. A. M. A. **122**: 1217-1224 (Aug. 28) 1943. Lockwood, J. S.; White, W. L., and Murphy, F. D.: The Use of Penicillin in Surgical Infections, Ann. Surg. **120**: 311-349 (Sept.) 1944. Roberts, J. E. H.; Tubbs, O. S., and Bates, M.: Pleural and Pulmonary Suppuration Treated with Penicillin, Lancet **1**: 39-45 (Jan. 13) 1945. Tillett, W. S.; Cambier, M. J., and McCormack, J. E.: The Treatment of Lobar Pneumonia and Pneumococcal Empyema with Penicillin, Bull. New York Acad. Med. **20**: 142-178 (March) 1944.

4. The anatomic conditions such as bronchial fistulas that cause constant reinfection of the cavity and allow the penicillin to escape must not be present. Bronchial fistulas, present more often than is generally realized, not only permit constant contamination of the cavity by organisms from the mouth but make it impossible to keep penicillin in the empyema.

5. The lung must be capable of reexpanding. Since reexpansion of the lung is the means by which empyema is cured it is obvious that, if the lung is not capable of reexpanding, aspiration of pus and instillation of penicillin will not suffice to heal the lesion.

There is no doubt that penicillin when properly used will obviate the need of surgical drainage in certain cases of empyema. Those responding to penicillin are chiefly the cases that have been detected relatively early when the pus is still thin and those in which none of the complications described are present. There is also no doubt however that, even when the complications described are present, penicillin can be of considerable aid as an adjunct to surgery. By means of penicillin and aspiration a large empyema can often be transformed into a small one that the lung can obliterate more quickly after rib resection. It is also possible to tide a critically ill patient over a period during which surgical intervention is hazardous. However, if the empyema is not bacteriologically and anatomically such that it will respond to penicillin therapy, to persist with aspiration of pus and instillation of penicillin is useless. An empyema is cured by expansion of the lung. Once the pleura becomes so thick that the lung cannot reexpand, an empyema cannot be cured by any means short of an operation designed to move the chest wall in to meet the lung. Such a procedure is serious and deforming and often must be done in stages. Drainage of an empyema by resecting a small section of rib under local anesthesia is such a trivial procedure compared to the operation for obliteration of chronic empyema that one is not justified in risking the possibility of having to do the latter in hopes of avoiding the former. It is rational then to treat an empyema by aspiration of pus and instillation of penicillin as long as rapid improvement is being made. If the patient becomes afebrile and the fluid decreases in amount, becomes sterile on culture and resembles the penicillin that was injected, satisfactory progress is being made. However, if the patient has a persistent fever, if the pus continues to accumulate and if the cavity fails to decrease rapidly in size, surgical drainage should be accomplished without further temporizing.

To summarize, use penicillin:

1. To cure small empyemas without loculation, lung sequestrums or bronchial fistulas.
2. To make large empyemas smaller.
3. To tide over a critically ill patient until he can be operated on safely.

The following cases, selected from those that have been treated with penicillin at the City of Detroit Receiving Hospital, illustrate these points:

REPORT OF CASES

Case 1.—C. M., a Negro aged 39, was admitted on April 15, 1944 with multiple stab wounds, one of which involved the left chest wall, the diaphragm and the stomach. Because the patient had consumed a large meal and considerable alcohol shortly before injury, his stomach was full and there was extensive soiling of the peritoneum. The wounds were repaired, and the chest and abdomen were closed without drainage. Postoperatively a pleural effusion developed on the left. On the fifth day following injury the abdominal wound disrupted. This was resutured under general anesthesia. The temperature, which had been elevated from the time of the first operation, remained elevated. On May 8, twenty-two days after admission, 60 cc. of pus was obtained from the left pleural cavity. Nonhemolytic streptococci and unidentified anaerobic cocci were recovered from the pus. The streptococci were sensitive to 0.04 unit per cubic centimeter of penicillin in vitro; the sensitivity of the anaerobic cocci to penicillin was not tested. Beginning on May 12 the empyema was aspirated daily and each aspiration followed by the instillation of 50,000 units of sodium penicillin in a few cubic centimeters of saline solution. The pus maintained its purulent character but gradually decreased in amount. On June 10, only 1 cc. could be obtained, and no further aspirations were done. The temperature became normal after thirteen days of therapy, and the patient has remained well to date.

Cultures of the pus were as follows:

May 8 and 13, nonhemolytic streptococci and unidentified anaerobic cocci.

May 14, aerobic gram positive spore forming bacilli.

May 17 and 25, nonhemolytic streptococci and unidentified anaerobic cocci.

June 4 and 9, no growth.

In this instance the empyema was small, was not loculated, was easily aspirated and was caused by organisms susceptible to penicillin. Aspiration of the pus followed by instillation of pencillin was therefore sufficient to cure the lesion. However, it required twenty-three days to sterilize the empyema and thirty days of therapy in spite of the sensitivity of the streptococcus to penicillin. The morbidity was about equal to that which would have accompanied surgical drainage; hence, while the treatment was successful, it had no great advantage over surgery. If, on the seventeenth day, it had been decided to do a rib resection because the pus had not yet been sterilized, the period of morbidity would have been longer than thirty days. Often during the treatment of empyema with penicillin it is difficult to decide whether the therapy is effective. Sometimes the patient improves clinically but the pus does not become sterile. At other times the pus becomes sterile but the patient remains febrile. Under such circumstances it is difficult to decide whether persistence in the treatment will result in a cure or whether rib resection will ultimately be necessary. If one resorts to rib resection after three weeks of penicillin therapy, the period of morbidity is prolonged. However, if one persists for many more weeks, one is risking the occurrence of chronic empyema if the treatment is not effective. The next case illustrates these difficulties:

Case 2.—J. B., a white man aged 51, was admitted on Feb. 18, 1944 with type II pneumococcic pneumonia involving the right lower lobe. Treatment with sulfamerazine resulted in a slight improvement, but the patient's temperature remained elevated. On March 1 250 cc. of thick pus yielding a type II pneumococcus was aspirated from the right pleural cavity. Following removal of the pus, the patient's temperature fell to normal and remained normal until March 6, when it rose again to 102-103 F. On March 6 the empyema was aspirated and 50,000 units of penicillin was instilled into the cavity. Aspiration and instillation were repeated twice daily for three days and then once daily for sixteen more days until March 25. Cultures of the pus during this period were as follows:

March 6 and 7, type II pneumococci.

March 8, 9, 10, 12, 13, 14 and 15, sterile.

March 24, type II pneumococci.

Although the pus appeared to become sterile shortly after the instillation of penicillin, the patient did not improve clinically. His temperature remained elevated and pus continued to

accumulate. In spite of the large amount of pus that was present, it was often difficult to withdraw much with a syringe because, as was subsequently shown at operation, large clots of fibrin blocked the needle. Since the patient failed to improve, it was decided to supplement the local instillation of penicillin with penicillin given intramuscularly. From March 14 to March 25 the patient received 10,000 units of penicillin intramuscularly every two hours in addition to the daily injection of 50,000 units in the empyema. During this regimen his temperature approached but did not reach normal, and the pus continued to accumulate. On March 24, after six negative cultures, pneumococci were again recovered from the pus. Accordingly it was decided to do a rib resection. Operation on March 28 disclosed a large cavity containing almost a liter of thick pus in which were many huge clots of fibrin. The pus obtained at operation was sterile. The character of the pus and the presence of fibrin apparently had prevented aspiration of the cavity.

This patient required rib resection after three weeks of very intensive penicillin therapy. The cavity was unilocular and easily accessible but contained so much thick material that it was impossible to aspirate the pus properly. The probable location of the pneumococci in the protected meshes of the fibrin was perhaps responsible for the positive culture on March 24, after twenty days of therapy, and for the continued accumulation of pus. Sixty-five days were required for healing. In this case reliance on penicillin prolonged rather than shortened the period of morbidity.

Case 3 illustrates the improvement that penicillin therapy can bring about in putrid empyema, but it at the same time illustrates one of the dangers of this form of treatment. The patient, feeling so much better because of the therapy, refused operation and left the hospital while viable streptococci could still be recovered from the pus in his chest. He may well develop chronic empyema.

CASE 3.—H. W., a white man aged 64, was admitted complaining of pain in his right chest of three days' duration. He had signs of right lower lobe pneumonia, but no pneumococci were found in the sputum. His temperature ranged between 100 and 102 F. He developed fluid in the right pleural cavity, and on Oct. 19, 1944 the chest was aspirated and a large quantity of pus obtained. Alpha hemolytic streptococci were recovered on culture. Unfortunately no anaerobic cultures were made, but the foul character of the pus indicated that anaerobes must have been present. There was some delay in obtaining penicillin, so the chest was not aspirated again until October 25, when 1,500 cc. of very foul pus resembling pea soup in appearance was obtained. Following the aspiration, 50,000 units of penicillin in about 80 cc. of saline solution was instilled in the empyema. On October 27 550 cc. of pus, which was no longer foul, was obtained. The temperature fell to normal on this day and remained normal for the rest of the hospital stay. Aspiration of pus and instillation of 50,000 units of penicillin was done daily until November 9. Although the fluid decreased in amount, only about 100 cc. being obtained the last few times it remained purulent and, except for an isolated sterile culture on November 2, always contained viable streptococci. On November 9, after two weeks of therapy, rib resection was advised, but the patient felt so well that he refused operation. Penicillin therapy was stopped. Aspiration on November 23 yielded 50 cc. of thin, brown, odorless fluid from which streptococci were grown on culture. Aspiration on December 4 yielded only 4 cc. of fluid, but on December 7 30 cc. was obtained. X-rays still revealed an encapsulated empyema.

On December 8 the patient left the hospital against advice. Although the empyema may in this case go on to resolution, the patient left the hospital with fluid which still contained streptococci in his pleural space. It is well known that such lesions may remain quiescent for months or even years and then flare up. We are inclined to believe, therefore, that eventually the patient will develop chronic empyema. There is no doubt that penicillin improved this patient's condition by reducing the size of the empyema and by killing the anaerobes, which were apparently originally present in the pus. If rib resection had been done when his chest contained 1,500 cc. of foul pus, a long time would have been required for reexpansion of the lung. However, if rib resection had been done after reduction in the size of the empyema cavity by one to two weeks of penicillin therapy, expansion would have occurred rapidly. Used to reduce the size of an empyema before operation, penicillin is of considerable value.

CASE 4.—O. H., a white man aged 47, was admitted on Oct. 9, 1944 with multiple stab wounds, one of which had entered the peritoneal cavity, lacerating the omentum and the liver. The patient had consumed sufficient alcohol to make him very uncooperative, and it was necessary to use general anesthesia in order to keep him quiet enough to permit repair of his wounds. Postoperatively he developed pleural effusion on the right. On October 20 aspiration of the right pleural cavity yielded 1,100 cc. of thin, brown fluid. No culture was made. The patient's temperature at this time was 101-102 F. Treatment with sulfadiazine was begun, the initial dose of 4 Gm. being followed by 1 Gm. every four hours. The temperature declined over a three days period to 99-100 F., where it remained until November 1, when the chest was again aspirated. Only a small amount of very thick pus was obtained. Type VIII and type XV pneumococci were recovered from the pus; 50,000 units of penicillin was injected into the empyema. Aspiration followed by injection of 50,000 units of penicillin was repeated daily until November 6, The cultures became negative after twenty-four hours of therapy. The temperature also fell to normal after twenty-four hours of therapy and remained normal. The patient has remained well to date.

This patient was treated successfully by only a few injections of penicillin. The good response in this case, as in the following one, was probably due to the small size of the empyema and the susceptibility of the organisms to penicillin.

CASE 5.—E. S., a white man aged 42, was admitted on March 28, 1944 for treatment of peritonitis caused by perforation of a peptic ulcer three days previously. Although his temperature was only 99-100.6 F. the patient was critically ill. On April 5 his temperature rose to 103 F. and he developed signs of a subdiaphragmatic abscess. On April 8 the posterior subdiaphragmatic area was explored; no definite pus was encountered, but the entire area contained fresh fibrinous adhesions between which were collections of clear fluid. There was no improvement following the operation, and by April 12 pleural effusion had developed. The temperature remained elevated. Fluid was aspirated from the right chest on April 14, but it clotted rapidly and no cultures were made. On April 17 the anterior subdiaphragmatic space was opened and a large abscess drained; beta hemolytic streptococci and Escherichia coli were recovered. Following drainage the patient's condition improved somewhat, but his temperature continued to rise and it was obvious that another collection of pus was present. On May 1 200 cc. of thin pus was aspirated from the right pleural cavity. Beta hemolytic streptococci, which were sensitive to 0.01 unit of penicillin per cubic centimeter, were recovered from the pus. On May 5 aspiration was repeated and 40,000 units of penicillin was instilled in the cavity. Aspiration and instillation were repeated daily for three days, and then 50,000 units of penicillin was injected daily for four days. The pus became sterile after the first twenty-four hours of treatment and decreased rapidly in amount. The last attempt at aspiration on May 15 yielded only a few cubic centimeters of fluid. The empyema has not recurred.

CASE 6.—V. B., a white woman aged 26, admitted on May 15, 1944, had had a pelvic operation three weeks prior to admission at another hospital, following which some sort of pulmonary complication occurred. This had not subsided, and she was acutely ill when she was admitted to the Detroit Receiving Hospital. On May 17 200 cc. of very foul, green pus was aspirated from the right pleural cavity. An anaerobic nonhemolytic streptococcus and alpha hemolytic streptococci were cultured from the pus. On May 20 the patient suddenly became critically ill. She was cyanotic and dyspneic and on physical examination exhibited not only signs of hydropneumothorax on the right but also numerous moist rales throughout the left lung. Her temperature was 104 F. It was believed that she had developed a bronchopleural fistula and had soiled the left lung with pus from the empyema. The empyema was completely aspirated and 50,000 units of penicillin was injected. Aspiration and instillation were repeated daily for thirteen days and the patient was also given 10,000 units of penicillin intramuscularly every hour for twenty-two days in order to control the soiling of the left lung. The patient's general condition improved slowly. Twenty-four hours after the onset of therapy the temperature fell to 100-101 F., where it remained for nine days before leveling off at normal, 100 F. The pus that was aspirated decreased steadily in quantity, lost its foul odor and changed to a thin brown fluid. The cultures were as follows:

May 19 and 20, 1944 alpha hemolytic streptococci and anaerobic nonhemolytic streptococci.

May 23, aerobic gram positive spore forming bacilli.

May 24, 25 and 27, sterile.

Although the empyema decreased in size, the bronchopleural fistula prevented the lung from reexpanding completely, and the patient continued to have a low grade fever. On May 8 a rib resection was done. This disclosed a small empyema into which there were several bronchial openings. Cultures from the walls of the cavity yielded anaerobic nonhemolytic streptococci.

In this instance penicillin therapy apparently saved the life of a critically ill patient. The penicillin that was given intramuscularly controlled the infection in the left lung, while further soiling was prevented by a combination of aspiration of the empyema and instillation of penicillin. By these means the patient's condition was improved and the size of the empyema was greatly reduced. When rib resection was finally done it was a simple procedure in a patient who was in good condition.

The next case illustrates a similar but more complicated problem:

CASE 7.—E. S., a white man aged 39, was admitted on Oct. 21, 1944 with type II pneumococcic pneumonia involving the right lower and middle lobes. He had been ill at home for seven days. At the time of admission his temperature was 105 F. and he was comatose. Because of his serious condition he was treated with penicillin, receiving an initial dose of 30,000 units intravenously and 20,000 units intramuscularly. This was followed by 15,000 units intramuscularly every three hours for fourteen days. Over the course of a week the temperature gradually fell to levels of 99-100 F. and considerable improvement had occurred. On November 4, when penicillin was discontinued, his temperature rose abruptly to 102 F. and remained at about this level until November 10, when it again fell almost to normal. In spite of the lowered temperature he continued to show anorexia, lethargy, a cough and weakness. During the next few weeks he improved slightly but had periods with a relatively normal temperature alternated with periods of fever. Because of the persistent signs of infection, consolidation of the right lower lobe, the absence of demonstrable empyema and x-ray evidence suggestive of multiple abscess formation, it was decided to reinstitute systemic penicillin therapy. On November 29 an initial dose of 20,000 units was given intramuscularly followed by 15,000 units every three hours. Penicillin was continued until December 17. On December 2 fluid was detected in the right pleural space and aspiration yielded 30 cc. of thick pus from which Staphylococcus aureus was recovered. Following aspiration 50,000 units of penicillin was instilled into the empyema. This procedure was repeated daily until December 11. Considerable difficulty was encountered in aspirating the empyema. At times 20 to 30 cc. of pus was obtained, while at other times nothing could be aspirated. It was apparent that a bronchial fistula existed, since the patient coughed and expectorated some of the solution each time it was injected.

In spite of systemic administration and the instillation of penicillin directly into the empyema, the patient failed to improve, and on December 12 a rib resection was done. The findings at operation were adequate to explain both the difficulties encountered at aspiration and the failure of the patient to improve. The empyema was fairly large, extending from the posterior axillary line to the paravertebral region and from the seventh to the ninth rib. There were several bronchial fistulas opening into the cavity, which contained a piece of necrotic lung about 3 inches in diameter. Traversing the cavity were several large vessels that could have given rise to a fatal hemorrhage at any time. Aspiration had been difficult for two reasons: (1) bronchial fistulas had provided sufficient drainage to prevent the accumulation of any great quantity of pus; (2) a lung sequestrum had covered the needle, making it impossible to aspirate either air or pus through it. Under such circumstances penicillin therapy could not have been expected to cure the lesion. Furthermore, the constant hazard of severe hemorrhage from the vessels traversing the cavity made it dangerous to delay surgical treatment.

The next case demonstrates the seriousness of delaying surgical drainage when large vessels traverse an abscess cavity.

CASE 8.—E. B., a Negro woman aged 23, admitted on Oct. 29, 1943 with an abscess near the base of the left upper lobe, had had a tonsillectomy six weeks previously. Pleural effusion developed; the patient became extremely dyspneic and had frequent small hemoptyses. On November 9 200 cc. of foul, thin, purulent fluid was aspirated from the left pleural cavity. Anaerobic hemolytic streptococci, anaerobic nonhemolytic streptococci and several unidentified anaerobic bacilli and cocci were recovered from the pus. Penicillin therapy was initiated on November 10. Ten thousand units was injected into the empyema daily, and 50,000 units was given intramuscularly every hour for twelve hours. The dose was then reduced to 10,000 units intramuscularly every hour. This was continued for fifteen days.

Improvement was slow but progressive. The amount of sputum decreased, the patient was able to dispense with the oxygen tent, and her appetite improved. The foul odor promptly disappeared from the fluid aspirated from the chest, and anaerobic streptococci were not recovered from it after the fourth day of therapy. Because of a shortage of penicillin the dose was decreased on the morning of the twelfth day to 5,000 units per hour. On November 22, the thirteenth day of treatment, only a small amount of sterile fluid was obtained on aspiration, and the temperature became normal. On November 23, the fourteenth day, it was necessary to decrease the dose again, and from this time until her death she received only 2,500 units every two hours. On November 25, the sixteenth day, she felt worse, and her temperature rose. That evening she had a fatal hemoptysis. At autopsy the empyema was found to be completely obliterated. An abscess about 1 inch in diameter was present in the left upper lobe and was surrounded by considerable consolidated lung containing many small abscesses. A large eroded vessel traversed the cavity.

This case might be considered a success so far as treatment of the empyema was concerned, and it illustrates the remarkable improvement that can be obtained in critically ill patients through the use of penicillin. It also illustrates, however, that penicillin cannot be

expected to correct certain anatomic changes; when these are present, surgical intervention should be prompt.

CASE 9.—G. G., a white man aged 63, who had been a tramp all his life, admitted to the hospital on Nov. 15, 1944 with a massive pleural effusion, had been ill for over a month, but he could not give a satisfactory account of his illness. He was very malnourished. On November 20 1,650 cc. of rather thin, foul, purulent fluid was aspirated from the right chest. More fluid was present, but the patient became so weak that aspiration had to be discontinued. Cultures of the fluid yielded beta hemolytic streptococci. On November 22 930 cc. of foul pus was aspirated and 50,000 units of penicillin instilled in the empyema. Aspiration and instillation were repeated daily for three days and then every other day for twenty-three days. The amount of fluid that could be aspirated decreased from 1,440 to 250 cc., and the cultures became negative on the tenth day of therapy. The patient did not improve a great deal, however. He continued to have a temperature of 99 to 100 F., his appetite was poor and he developed diarrhea. No cause for the diarrhea could be found.

Because of the persistent accumulation of pus after twenty-three days of therapy, failure of the cavity to decrease significantly in size during the last week of therapy and the patient's persistent poor condition and low grade fever, rib resection was done under local anesthesia on December 16. The cavity held about 250 cc. and was unilocular. Following operation beta hemolytic streptococci were again recovered from the empyema. The patient's course after operation was progressively downhill, and he died on Jan. 6, 1945. Death was due to multiple pulmonary infarcts. The empyema itself was progressing well.

This patient was in extremely poor condition when he was admitted to the hospital, and the delay of seven days between admission and the onset of therapy did not improve it. Whether the outcome would have been different if treatment had been instituted earlier or if surgical drainage had been done is not pertinent to this discussion. The point is that in an empyema of this size and duration twenty-three days of penicillin therapy were not adequate to effect a cure. During the last week of treatment pus continued to accumulate, and the cavity did not decrease in size.

CASE 10.—B. W., a white girl aged 2 years, was admitted on Jan. 3, 1944 with postpneumonic empyema, bronchopleural fistula and tension pneumothorax. Intercostal drainage was done the next day, releasing purulent fluid under pressure. Cultures showed type III pneumococci. Sulfamerazine therapy for the next fifteen days resulted in little or no improvement, and on January 18 penicillin was begun. Cultures yielded a coagulase positive Staphylococcus albus, which was sensitive to 0.156 unit of penicillin per cubic centimeter. Four thousand units of penicillin was injected intramuscularly every hour, and 40,000 units of calcium penicillin was instilled into the empyema cavity every twelve hours. The intercostal catheter was clamped off after each instillation of penicillin and was opened again one hour before the next injection. When there was no change in the patient's condition after six days of penicillin therapy a rib resection was done. Immediately the temperature fell to normal, and improvement was steady thereafter. Penicillin was discontinued three days after the operation.

In this case penicillin was of no value as far as could be determined. Failure to cure the lesion was to be expected in the presence of a bronchial fistula, but one would have expected some improvement in the child's general condition as a result of the therapy.

CASE 11.—J. C., a white man aged 67, was admitted on Dec. 15, 1944 with a putrid empyema known to be of at least three weeks' duration. On December 16 550 cc. of foul pus was removed. There was no growth aerobically, but a smear of the pus showed that it contained staphylococci, streptococci and diphtheroids. No anaerobic culture was made. On December 18 900 cc. of pus was removed and 100,000 units of penicillin was instilled. At this time the patient's temperature was 102 F. Aspiration of pus was repeated on December 19, 20, 21 and 23, 100,000 units being instilled on December 19 and 50,000 units thereafter. The pus lost its foul odor but did not decrease in amount, and the patient continued to have a temperature of 101-102 F. He developed abscesses in the chest wall at the sites of aspiration, so penicillin was discontinued and the empyema was drained.

It is possible that the patient might have responded to penicillin if treatment had been continued. However, his course during the first five days did not seem to indicate that this would occur, and in view of the infection in the chest wall it seemed safer to resort to surgical treatment.

CASE 12.—L. R., a colored woman aged 20, admitted on Jan. 20, 1944 suffering from disseminated lupus erythematosus, developed pneumonia of undetermined etiology in the left lower lobe on February 10. This improved somewhat with sulfamerazine therapy, but an effusion occurred and persisted. On March 2 1,500 cc. of green pus was aspirated from the left pleural cavity. Alpha hemolytic streptcocci, which were inhibited by 0.02 unit of penicillin per cubic centimeter, were recovered from the pus. On March 9 and for sixteen days thereafter the empyema was aspirated daily, and 50,000 units of penicillin was instilled after each aspiration. The pus became sterile after two days of therapy, and the amount of fluid that could be aspirated decreased rapidly. Small loculated collections of fluid formed that could be seen in the x-ray films for a month after treatment had been stopped, but these slowly disappeared. The patient died on June 30 from other causes. At autopsy the empyema cavity was found to be obliterated except for one very small collection of 8 to 10 cc of purulent appearing material. This was sterile on culture.

This case was successfully treated probably because of the extreme sensitivity of the infecting organism to penicillin. If the organism had been more resistant, it would have persisted in the loculation that formed and would have prevented a successful outcome.

CASE 13.—E. W.,[4] a white woman aged 26, was first admitted to the hospital in October 1943 with bilateral pulmonary tuberculosis and a large cavity on the right. Attempts to collapse the lung and obliterate the cavity were unsuccessful, so an intrapleural pneumolysis was done in two stages soon after the patient's admission. On December 13 x-rays for the first time showed fluid collected at the right base. On Jan. 19, 1944 the temperature suddenly rose to 104 F. and the patient experienced frequent chills. There was concurrent increase in the amount of fluid, and the patient became very ill. Aspiration and culture revealed no organisms, but anaerobic cultures were not done. The cavity in the lung was well collapsed, and the patient was responding well as far as the tuberculosis was concerned. Because of this good response and also because the disease was bilateral, her physician did not want to give up the pneumothorax. Consequently it was maintained, and the pleural cavity was aspirated frequently. The fluid became foul and increased in amount until 1,500 cc. was being aspirated every few days. At each aspiration the cavity was irrigated with saline solution and 50 cc. of hexylresorcinol was instilled.

On February 19 1,000 cc. of fluid was aspirated and 50,000 units of calcium penicillin was instilled. The fluid at this time was particularly foul, and cultures yielded an anaerobic streptococcus, unidentified anaerobic cocci and organisms resembling diphtheroids. Penicillin was injected twice daily for the next nine days, during which time the fluid became odorless and decreased in amount. From February 28 to March 6 the patient

4. This case is reported with the permission of Dr. W. A. Hudson.

received intravenously 100,000 units of sodium penicillin daily and then 50,000 units intravenously every day to March 13, when all medication was stopped. During this time the temperature came down and the patient gained weight and felt very well; the temperature remained normal with only occasional rises to 100 F. On March 21 the phrenic nerve was crushed. The temperature again rose on April 3 and the fluid became purulent. On April 14 225 cc. of thick greenish pus was aspirated, and after saline irrigation 50,000 units of sodium penicillin was instilled in 100 cc. of saline solution. This amount was repeated daily until April 24, then 50,000 units every two days to June 2, and then once weekly until June 26. During this time the amount of fluid aspirated varied between 150 and 200 cc. Cultures yielded anaerobic cocci and diphtheroids. The temperature at the time penicillin was started on April 14 was varying from 100 to 101 F. During the rest of April the temperature varied from normal to 100 F., with occasional rises to 101 F. and one to 103 F. Through May, however, the temperature was higher than 99 F. on only two occasions.

After penicillin was stopped, 100 to 150 cc. of fluid was aspirated occasionally through July 24. Cultures were sterile until this date, when an anaerobic nonhemolytic streptococcus was again found. The cultures are listed as follows:

Feb. 19, 1944, anaerobic diphtheroids; gram-positive rods.
February 21, anaerobic gram-positive rods.
February 25 and March 1, 4, 6, 8, 10 and 13, sterile.
March 27, anaerobic cocci.
April 11, anaerobic gram-positive rods.
April 15, anaerobic cocci; diphtheroids.
April 17 and 22, sterile.
April 24, anaerobic cocci.
May 1, anaerobic gram-positive cocci; anaerobic streptococci.
May 8, sterile.
May 15, anaerobic gram-positive rods and diphtheroids; aerobic alpha streptococci and diphtheroids.
May 22, sterile.
May 29, anaerobic cocci; Alcaligenes sp.
June 5, 6, 19 and 26 and July 3, sterile.
July 24, anaerobic nonhemolytic streptococci.

During the next six months the patient improved slowly. Penicillin in doses of 25,000 units to 50,000 units intrapleurally was necessary biweekly to prevent the reaccumulation of fluid. During this time it was finally decided to do an upper stage thoracoplasty; this was done in September 1944. The wound healed by first intention and at present, February 1945, the patient has only a small empyema cavity remaining and is about to be discharged to her home.

This case illustrates the value of penicillin in holding a putrid empyema in check, but it also illustrates the fact that an empyema is cured only when the cavity is obliterated. This may be accomplished by reexpansion of the lung or, as in this case, by moving the chest wall in to meet the lung. Any chemotherapy that is not accompanied by obliteration of the empyema is bound to fail.

Poisonous Spiders.—Tarantulas of the United States cannot be accepted as a menace. They are slow to attack a human being, are not numerous, and their poison lacks potency sufficient under normal circumstances to produce permanent or even serious harm. Mankind has reacted in some instances to poison secreted by certain species, as the giant Mygales of South America, but simple, local treatment is usually all that is necessary to offset the temporary effects. The bite of Atrax robustus of Australia, however, may cause serious symptoms and, under certain conditions, death to man. Fortunately this species is limited in its range; hence few instances of this kind are on record. The most universally distributed "dangerous" spiders are those of the genus Latrodectus, and it is they, more than all others, which are responsible for serious cases of spider bite.—Thorp, Raymond W., and Woodson, Weldon D.: Black Widow—America's Most Poisonous Spider, Chapel Hill, University of North Carolina Press, 1945.

OCULAR MALDEVELOPMENT IN EXTREMELY PREMATURE INFANTS

RETROLENTAL FIBROPLASIA: VI. GENERAL CONSIDERATION

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In 1941 it was recognized that a massive growth of embryonic connective tissue occurring in the meshwork of a persistent tunica vasculosa lentis is linked with prematurity.[1] To my knowledge there are at least 162 cases at the present time. Dr. Stewart Clifford[2] has found that 12 per cent of the infants weighing 3 pounds (1,360 Gm.) or less at birth develop this disease. This percentage, based on less than 50 cases of prematurity, can be considered only a trend. If the true percentage of infants developing this disease is about 10, approximately 600[3] cases are to be expected in this country each year, which, if some prophylaxis is not found, will add materially to the 175,000 blind.[4]

Typical well developed cases show seven characteristic findings:

1. There is opaque vascularized tissue behind the crystalline lens in which the vessels tend to radiate from a central point.
2. The eyes are abnormally small and as a result the eyelids, especially the lower, are sunken.
3. The anterior chambers are shallow, if not completely absent.
4. The irises retain their fetal-blue color, changing slowly to an abnormal gray-blue or dirty brown color.
5. Thin ciliary processes, appearing like teeth of a comb, can be seen in front of the opaque tissue when one looks through the dilated pupils from the extreme periphery.
6. The eyes have a searching nystagmus.
7. There is an apparent photophobia characterized by the infants covering the eyes when exposed to a brilliant light.

Frequently openings are seen in the opaque tissue through which one can observe the persistent hyaloid artery crossing the eye from the nervehead to the back of the lens. In some instances the opaque tissue seen at one side, through partially uninvolved vitreous, appears to have appreciable depth, extending posteriorly, often reaching the retina itself. Retinal separation may be and, at times, is the most obvious ocular disturbance.

Attempts to produce the disease in pouch young of the opossums and in newborn rats have failed, as have measures calculated to cause precocious closure of the hyaloid artery and tunica vasculosa lentis system. Although the pouch young of the opossum and newborn rats furnish immaturely developed eyes, it is possible

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1. Terry, T. L.: Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants: Preliminary Report, Am. J. Ophth. **25**: 203 (Feb.) 1942; II. Report of Cases, Arch. Ophth. **29**: 36 (Jan.) 1943; III. Embryological Studies, Am. J. Ophth. **29**: 1409 (Dec.) 1942.
2. Clifford, Stewart: Personal communication to the author.
3. The number of cases is necessarily an estimated figure. Of the 125,671 premature births yearly in this country, as indicated from Vital Statistics (**19**: 2 [Dec.] 1943), approximately 22,888 are extremely premature. If the true survival rate is represented by that of Hess and his associates at 43 per cent, then 11,131 should survive. If even 10 per cent of the survivors develop fibroplasia there should be over 1,000 cases per year. Because this statistical approach is founded on relatively meager numbers of reports of survival and of development of fibroplasia, subtracting 40 per cent for possible gross errors there would still be at least 600 per year.
4. Commonwealth of Massachusetts, Division of the Blind: Personal communication to the author.

that the failures to produce the disease can be attributed to eye characteristics different from those of the human being.

The hyaloid vascular system ceases to carry blood eight and a half months after conception,[5] and infants born earlier than this have a functioning hyaloid vascular system. In this meshwork the embryonic connective tissue can develop, thus producing retrolental fibroplasia. Because the disease process is not present at birth, developing from two to six months later, some factor resulting from premature birth must be responsible. It should be noted, however, that occasionally this condition, or one similar to it, usually unilateral, may be found at birth in the full term infant, having developed during intrauterine life. The ratio, since 1941, of fibroplasia in the premature and in the full term infants has been 162:4. Formerly, eyes involved with this disease were frequently considered to be eye cancers (retinoblastomas), thus warranting enucleation. The rarity of fibroplasia in the full term infant over the years is further shown by only 5 laboratory specimens in the collection of 12,000 enucleated eyes at the Massachusetts Eye and Ear Infirmary.

Many factors have been considered the probable cause of fibroplasia. These include heredity, intraocular inflammation, precocious exposure to light, precocious closure of the ductus arteriosus and the foramen ovale, an increase or decrease of oxygen in the blood, the lower temperature of the premature infants in the incubator in contrast to intrauterine fetal temperature, lack of adult maternal endocrine environment, precocious elevation of blood pressure, complications arising from the Rh factor differences in the mother and infant, inability to digest and assimilate food including vitamins, trauma or intraocular hemorrhage introducing the process, intraocular inflammation or infection, physiologic anemia of prematurity, changes in the blood such as premature establishment of the characteristic blood group and, finally, the causes of prematurity itself.[6]

Certain trends in biologic experiments indicate, but by no means prove, that the precocious exposure to light[7] may be the most important factor. The effects of light in exciting the disease process would more probably be related to the motor responses to light than to the stimulation of the retinal receptors. Animals whose eyes are extremely undeveloped at birth have their eyes sealed for a varying period after birth, and often light is further excluded by hair, usually dark, on the lids.[8] In the adult human being a pupillary response is obtainable in one opened eye when the light is carefully flashed so as to fall on the other closed eye, thus showing that sufficient light transilluminates the closed lid to produce a consensual pupillary reaction. Fibroplasia appears to occur more frequently in some places than in others. For example it is often found in one premature nursery, while other nurseries in the same city will have few if any cases. Similarly, 1 of twins, and in 1 instance 2 of triplets, have been known to develop the disease. The exposure to light varies with the frequency of examination and position in the nursery in relation to the location of the lights. Precocious light exposure as a possible cause can be determined most effectively if a fairly safe technic is worked out which will permit keeping the infants in the dark, or perhaps under a red light, and adequately covering the eyes while the infants are being examined or given nursing care under normal lighting conditions. Fibroplasia appears to be frequent enough to warrant bold measures, and it is my feeling that it is worth the risk to use a mydriatic or a miotic as a possible preventive measure. Which is better is open to conjecture, because the eyes in the dark have dilated pupils while in sleep the pupils are small. The status of the pupils in the fetus asleep and awake in the dark uterus can be different from the status of the pupils of the premature infant asleep and awake in the nursery, where it is in the light as much as or more than in the dark. That the pupil can react long before birth is indicated by the presence of small pupils and response to a mydriatic in premature infants weighing less than 2 pounds (907 Gm.). Ida Mann[9] states that the sphincter pupillae morphologically appears capable of activity in the four months fetus. The use of a mydriatic, preferably atropine because its effect is more permanent, would be the easier. In the use of both drugs, however, there is danger of favoring the development of complications, such as glaucoma with atropine or posterior synechia with pilocarpine. If, in using atropine in one eye only, no difference in the frequency of development of fibroplasia is observed in the two eyes of 50 or more premature infants so handled, this drug could be discarded as a preventive measure. The same procedure could be tried with miotic drugs, but one should remember that their effect is temporary, lasting perhaps not over two hours at best.

Treatment through direct surgical attack, through use of radiation or through an attempt to seal the hyaloid artery with diathermy has ended disastrously. If no treatment is given, in some instances there is a spontaneous reduction in amount of opaque tissue, but the eyes usually fail to grow normally. At times cataract and corneal opacities develop in addition to glaucoma and posterior synechia, which have been previously mentioned. Despite the ability in all extremely premature infants to see these fetal vessels of the hyaloid artery and tunica vasculosa lentis, which should normally disappear, it has not been possible as yet to determine which of the premature infants will develop the disease. As the fibroplasia develops after the infant has completed its incubator life and has been discharged to its home, many stages of the development have not been observed.

To prevent the development of glaucoma after the disease has arisen, a miotic, usually 1 per cent pilocarpine, is used daily. As there is a tendency for posterior synechia to develop, a combination of powerful synergistic mydriatics[10] which keeps the pupil dilated only a few hours is used once weekly. One drop of this medicine suffices. The parents are advised to observe the eyes after mydriasis to see if the pupil fails to dilate or to note any tendency of the pupil to be unround, an evidence of synechia formation. These preventive measures appear to lessen the frequency of two dangerous complications.

		Gm. or Cc.
10. ℞	Homatropine hydrobromide	0.15
	Epinephrine bitartrate	0.30
	Cocaine hydrochloride	0.075
	Paredrine hydrobromide 1%	15.000

The operation, calculated to establish a new vascular connection between the episcleral vessels outside the eyeball with the ciliary body, has been performed on

5. Mann, Ida: The Development of the Human Eye, Cambridge University Press, 1928, p. 212.
6. Terry, T. L.: IV. Etiologic Factors, Arch. Ophth. **29**: 54 (Jan.) 1943.
7. Terry, T. L.: V. Further Studies, to be published.
8. Snyder, F. F.: Personal communication to the author.
9. Mann: Development of the Human Eye, p. 128.

several severely involved eyes, with probable beneficial effects in about half.

In giving guidance and advice to the parents, the following points are brought out: First, they must adjust themselves to the probability that their baby will not see; that blind people are happy people and can become normal, healthy, useful citizens. Second, the child should be given normal affection but should not be pampered, being treated as though normal. Third, toys that are interesting from the standopint of shape and sound should be provided. Fourth, companionship with other children of the same age should be sought. This can be obtained at blind baby nurseries. Fifth, music, which has been found almost invariably to be enjoyed and appreciated, should be given to these children, in some instances with music lessons. Sixth, school, on advice from the Perkins Institution for the Blind, is to be delayed until the seventh year.

As there is no suspicion that this is a hereditary disease, the parents are told that they should not be hesitant about having more children.

SUMMARY

Over 10 per cent of the infants born very prematurely, weighing 3 pounds or less at birth, can be expected to be blind from retrolental fibroplasia. If this percentage remains, at least 600 cases will occur annually, thus increasing the blind census materially.

The typical characteristics of the disease are opaque vascularized membrane behind the lens, microphthalmia, shallow anterior chambers, fetal-blue color of the iris, thin ciliary processes in front of the opaque tissue, searching nystagmus, apparent photophobia, persistent hyaloid artery and often retinal separation.

The basis of the disease lies in the presence of a functioning hyaloid artery and tunica vasculosa lentis system in all infants born even three or four weeks prematurely.

Of all the probable causes listed, precocious exposure to light is considered the most tenable, and preventive measures should be taken.

For prevention, mydriatics and miotics could be used but if considered too drastic the infants should be kept in a dark room with a red light and the eyes covered adequately during examinations and nursing care.

Treatment consists in preventing the most common complications glaucoma and posterior synechia by use of miotics and mydriatics. Surgical and radiation therapy have proved unsuccessful. A surgical attempt, however, to establish a new vascularization of the ciliary body with the episclera is being done with some beneficial results.

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ABSTRACT OF DISCUSSION

Dr. Heyworth N. Sanford, Chicago: No doubt those who have worked many years with the premature infant have been wondering why they never observed this eye dyscrasia. I observed 1 instance of retrolental fibroplasia in a premature infant weighing 2 pounds (907 Gm.) about two years ago. Since then Dr. Justin Donegan has also examined the eyes of all our premature infants, but we have failed to observe any more. This is not surprising and I would emphasize that Dr. Stewart Clifford observed that they occur in only 10 per cent of premature infants weighing 3 pounds (1,360 Gm.) or less. While the average obstetric service will run about 10 per cent of premature infants, the majority of these infants will be over 3 pounds in weight, as were those that we studied. As only about half a dozen of these were under 3 pounds, this would agree with Clifford's estimate of 1 in 10 premature infants of 3 pounds or less. When Dr. Ethel Dunham made her survey on the premature mortality in hospitals throughout the United States in 1930 she found that the average premature mortality was about 26 per cent. In Chicago from 1931 to 1937 Dr. Edith Potter reported that the premature mortality for Lying-In Hospital was 20.7 per cent. Since 1938 there has been a drive in Chicago as in many other cities to lower the premature mortality. Certainly the premature mortality now in those hospitals in Chicago which offer adequate premature care is well below 20 per cent. This means a reduction in ten years of approximately 8 per cent, and most of this decreased mortality has been in premature infants under 3 pounds. Premature infants that once were born in hospitals with no facilities for premature care or in the home and would thus die shortly are now removed to hospitals with facilities for premature care and are saved. I wonder if we are not having more of these very small premature infants to study, which prior to this time we did not have an opportunity of seeing under the conditions that we have today. While this is undoubtedly a new disease, it is one that has not before been apparent because the type of child carrying such a deformity has not heretofore been saved in sufficient numbers to demonstrate this condition. By increasing the span of life of the average adult through the last decades we have increased the incidence of some diseases. Here by saving the lives of very small premature infants that heretofore have perished we have likewise added another condition that we must now endeavor to find a therapeutic means of combating.

Dr. E. V. L. Brown, Chicago: Incubator care has saved many lives, but as a result of it, apparently, there are several hundred blind babies in the country. Previous to 1935 some sixteen eyes had been removed by me for glioma retinae—neuroblastoma—and all were gliomas. But in the next five years I was responsible for the removal of six more, four of which proved to be retrolental fibroplasia and not glioma and need not have been removed at all. Dr. Terry postulates that this condition may be due to faulty development of the ciliary body basically. The mother is almost always the one who discovers this condition. She usually, it seems, finds it while she is bathing the child and the light happens to strike the pupil just right and she sees the mass behind the pupil. Ordinary observation by other members of the family or by the family doctor or pediatrician may not corroborate what she has seen. We should give every mother who has a premature child, at least before the seventh month or of only 3 or 3½ pounds (1,360 to 1,587 Gm.) of weight instructions to watch carefully the child's eyes throughout the first year. I do not know of cases that have occurred later than the first year in which there is any evidence that the condition was not present before that. It is occurring in our large centers of population certainly in a considerable number of cases. The number that Dr. Terry has seen, around 100 in the neighborhood of Boston, seems to be huge, but the late Dr. S. R. Gifford had seen 15 or 20 cases. Dr. Gradle told me that he had seen some 15 cases. My colleague Dr. J. M. Donigan and I have seen between 15 and 20 cases. Dr. Richard Gamble has seen some 5 cases. So we are up to around 75 or 80 just among five or six of us here in Chicago, in the last couple of years.

Dr. A. J. Strich, Chicago: I should like to report briefly on a negative series of experiments on the etiology of fibroplasia conducted at the Children's Memorial Hospital in Chicago by Dr. Gamble and myself. We have seen in the past few years 16 cases of fibroplasia, and Dr. Terry has been in consultation on 2 of them. Working on the presumption that this disease, which used to be rare, suddenly became quite frequent in the last few years and on the presumption that these children are not born with fibroplasia but show it after a few months of their lives, we have surveyed several Chicago nurseries from which our 16 patients came, looking for the factor which made the disease common. We thought of sulfonamides, but only a few of our patients had had them. We thought of vitamin K, but only 1 or 2 of them had had it. But with only 1 exception all of these babies came from nurseries where the so-called germicidal lamp was employed. This is an ultraviolet ray producing lamp and it has been used for the past few years to

sterilize the air in nurseries. We decided to investigate this point experimentally. We received 12 female pregnant rats and used ten families as an experimental group which was exposed to the germicidal lamp. We set two families aside in a dark room. The germicidal lamp is a powerful lamp. Some of the families which received more irradiation were burned to death. The ones that received a little less irradiation survived but developed cataracts. Rats seemed to be animals which would be suitable for that experiment because rats are being born with a hyaloid system still present and they have blood vessels around the lens and these blood vessels disappear in from two or three weeks. The blood vessels continued to disappear in two or three weeks in our working group just as fast as in our control group, which might prove the point that either the germicidal lamp is not the cause of fibroplasia or that rats do not develop fibroplasia. However, we shall not give up and we intend to find out how many of the children throughout the country having fibroplasia were kept in nurseries where they were exposed to continuous light, be it germicidal or not.

DR. T. L. TERRY, Boston: Some of the points brought up are answered in previous publications, and others can be based on poorly supported conjecture.

INFLUENCE OF NEOSTIGMINE METHYLSULFATE ON PREECLAMPTIC PATIENTS

AND CHOLINESTERASE ACTIVITY OF PLACENTAS FROM NORMAL AND PREECLAMPTIC PATIENTS

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A number of reports [1] state that the normal pregnant woman has some substance in her blood which will neutralize posterior pituitary injection and that an injection of this substance into preeclamptic patients will occasionally initiate the onset of convulsions. The investigations of Schockaert and Lambillon [2] and of Dieckmann and Michel [3] demonstrated that approximately 65 per cent of preeclamptic and eclamptic patients show abnormally great and prolonged blood pressure elevations and antidiuretic responses to pitressin. Since the studies of Necheles and Neuwelt [4] indicate some antagonism between acetylcholine and pitressin, the question arose whether acetylcholine activity is altered or abnormal in eclamptic toxemia.

There are some data which suggest that a relative decreased acetylcholine activity may occur in preeclampsia. Human placentas contain large amounts of acetylcholine, as was shown by Chang and Gaddum,[5] who reported 28 micrograms per gram of fresh placenta. Hofbauer [6] reported acetylcholine values for five whole placentas of eclamptic patients and though no placental weights were given he concluded that these values were significantly lower than the normal values of Chang and Gaddum. Hofbauer [6] also quoted investigations at Harvard University to show that the cholinesterase activity of preeclamptic placentas was higher than normal. However, personal communication from the Harvard laboratory [7] indicated that the work which was quoted was incomplete and was not ready for publication. Therefore cholinesterase activity was determined in placentas from normal and preeclamptic patients.

The naturally occurring acetylcholine can be potentiated by inhibiting cholinesterase, the enzyme which destroys it. Neostigmine methylsulfate has this action. It seemed worth while to investigate the effects of this drug on preeclamptic patients, since preparations of veratrum viride, another parasympathomimetic drug, are useful in treatment of preeclampsia.

METHODS AND MATERIAL

Eight patients, pregnant seven to nine months, have been studied. Five were diagnosed preeclamptic and showed edema, proteinuria, visual disturbances and hypertension of recent origin. Two were hypertensive without evidence of any toxemias of pregnancy and 1 was a normal control.

The blood pressure studies were accomplished with the hypodermic manometer.[8] Neostigmine methylsulfate was administered until definite effects occurred. One to three intramuscular injections of 0.25 mg. at intervals of ninety minutes were followed at hourly intervals by one or two intravenous injections of 0.02 to 0.25 mg. The drug was discontinued whenever uterine activity started or whenever either the systolic or the diastolic pressure was elevated an additional 20 mm. of mercury. This method of administration was selected with four important facts in mind: (1) The susceptibility to the drug might vary greatly, (2) as with physostigmine [9] there might be an appreciable latent period even after intravenous injections, (3) the interference with the destruction of acetylcholine might allow liberation of sufficient amounts from the placenta to cause excessive and dangerous uterine activity and (4) preeclamptic patients might be abnormally susceptible to the stimulative action of the drug at prepostganglionic synapses of the sympathetic nervous system (nicotinic action).

Cholinesterase activity was determined in placentas of 8 normal and 13 preeclamptic patients by Torda's modification [10] of Glick's method.

RESULTS AND COMMENT

Individual susceptibility to neostigmine appeared to vary greatly. Pronounced effects were produced in 1 case with 0.25 mg. intramuscularly and 0.023 mg. intravenously, while in another case 1.00 mg. intramuscularly and 0.75 mg. intravenously was necessary to produce definite effects.

In the preeclamptic and the control patients uterine activity and vascular effects appeared rather suddenly

Aided by a grant from Eli Lilly and Company.
The neostigmine methylsulfate used in this study was supplied by Hoffmann-La Roche, Inc.
From the Department of Pharmacology and the Department of Obstetrics and Gynecology, University of Georgia School of Medicine.
Read before the Section on Experimental Medicine and Therapeutics at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

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2. Schockaert, J. A., and Lambillon, J.: New Test for Early and Differential Diagnosis of Preeclampsia in Pregnancy: Effect of Posterior Pituitary Preparation on Blood Pressure, Bruxelles-méd. **17:** 1468, 1937.
3. Dieckmann, W. J., and Michel, H. L.: Vascular-Renal Effects of Posterior Pituitary Extracts in Pregnant Women, Am. J. Obst. & Gynec. **33:** 131, 1937.
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8. Hamilton, W. F.; Woodbury, R. A., and Harper, H. T., Jr.: Physiologic Relationships Between Intrathoracic, Intraspinal and Arterial Pressures, J. A. M. A. **107:** 853 (Sept. 12) 1936.
9. Krayer, O.; Goldstein, A., and Plachte, F. L.: Quantitative Relation Between Dosage of Physostigmine and Inhibition of Cholinesterase Activity in the Blood Serum of Dogs, J. Pharmacol. & Exper. Therap. **80:** 8, 1944.
10. Torda, Clara: Cholinesterase Content of Tissues Without Innervation (the Placenta), Proc. Soc. Exper. Biol. & Med. **51:** 398, 1942.

after a definite latent period of ninety to one hundred and twenty minutes even after intravenous injections. In 1 normal patient and in 1 hypertensive patient neostigmine failed to lower the blood pressure though uterine activity was initiated. In the second hypertensive patient neostigmine elevated the arterial pressure. These observations indicate that small to moderate amounts of neostigmine do not lower the arterial pressure in control noneclamptic gravid patients even though hypertension may be present. They suggest that the drug may initiate labor during the seventh and eighth months, which differs from the reported absence of effect on the uterus when used as a pregnancy test early in pregnancy.[11]

In 3 of the 5 gravid preeclamptic patients neostigmine, after initially elevating the blood pressure 10 to 20 mm. of mercury, produced chill, a temperature elevation of 1 to 2 degrees F. and a reduction of the arterial pressure from 185/105 to 143/83, from 220/125 to 124/92 and from 145/82 to 100/60 (see plot of the arterial pressure of 1 case in figure 2). The arterial pressure remained low for four to eight hours until the action of the drug had diminished and until the excitement, activity and pain associated with labor had increased the blood pressure. In the other 2 preeclamptic gravid patients neostigmine not only failed to lower the blood pressure but in 1 of these it raised the pressure 20 mm. of mercury. These elevations could result from the stimulating action of acetylcholine on autonomic ganglions and of course are not beneficial to the patient. The fact that neostigmine sometimes lowers and sometimes increases the arterial pressure may be taken as indicating that there are several different types of preeclampsia; sometimes one altered physiologic process is important, while in other patients different processes may be altered to a larger extent.

One of the preeclamptic patients who showed a pronounced reduction in blood pressure from neostigmine was again tested ten hours post partum. At this time neostigmine failed to lower the arterial pressure (fig. 2). Adequate dosage had been administered, since 0.32 mg. of acetylcholine administered intravenously over a period of twenty seconds lowered the arterial pressure 40 mm. of mercury, while in the absence of neostigmine only minimal effects are produced by doses twenty to sixty times as large.[12] These data are interpreted to show that pronounced effects can be obtained from moderate amounts of neostigmine when administered ante partum. This is apparently due to the fact that a large depot of acetylcholine is present in the placenta. The neostigmine inhibited its destruction and allowed greater acetylcholine activity.

Preeclamptic placentas had a significantly greater cholinesterase activity than those of normal women. Values expressed as micrograms of acetylcholine chloride hydrolyzed per milligram of dried placenta per second were for normal women $6.0 \pm$ S. E. of 0.15 and for preeclamptic patients, $9.4 \pm$ S. E. of 0.19. Statistical evaluation showed that $t = 4.0$, which indicates that the probability of this difference occurring by chance is 1:12,000. The presence of the high cholinesterase activity in the placenta may be a protective mechanism or may be a contributing factor to the condition of preeclampsia.

As shown in figure 1, neostigmine increased the standing waves in the radial pressure pulses. This change of the pulse contour indicates that peripheral vasoconstriction occurred in the vessels of that arm.[13] Apparently muscular and cutaneous vessels were constricted. Intensive widespread cutaneous vasoconstriction could account for the chill but cannot account for the pronounced reduction in arterial pressure in these patients.

This generalized vasoconstriction should increase arterial pressure and retard blood outflow from the arterial tree. Since the blood pressure is reduced and since the rate of descent of pressure during the last part of systole is increased (figure 1) the outflow of blood from the arterial tree must actually be rapid. This rapid flow can be and probably was into the uterus and placenta.

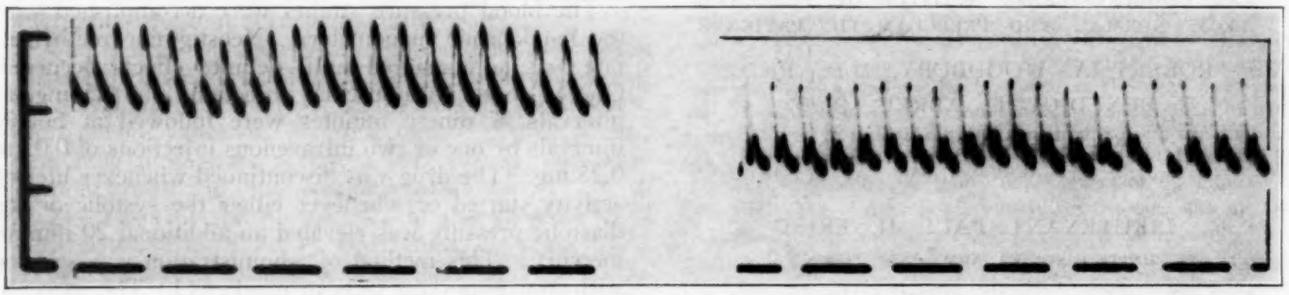

Fig. 1.—Radial pressure pulses from preeclamptic patient. Blood pressure scale is shown in units of 50 mm. of mercury. Base line is interrupted at intervals of two minutes. Tracing at left was recorded at 12 o'clock noon. Neostigmine methylsulfate was injected intramuscularly 0.25 mg. at 12:15 p. m. and intravenously 0.023 mg. at 1:15 p. m. Chill and uterine activity were present at 2:10 p. m. Tracing at right recorded at 2:30 p. m.

Provided this flow is augmented, any sudden interference with it would be expected to cause a definite increase in maternal arterial pressure. Each uterine contraction constitutes an interference with maternal uterine placental blood flow, since these hinder maternal blood flow into the uterine placental area and squeeze maternal blood from the uterine sinusoids.[14] The fact that in these patients at this time uterine contractions elevate the maternal arterial pressure 40 to 50 mm. of mercury during systole and 20 mm. of mercury during diastole provides proof that maternal uterine placental blood flow and volume are large. Control postpartum neostigmine administrations did not significantly alter the arterial pressures in these patients.

These data can be interpreted as evidence that neostigmine administered to preeclamptic gravid patients decreases the blood flow to muscle and cutaneous areas and in some patients increases blood flow to the uterus

11. Soskin, S.; Wachtel, H., and Hechter, O.: Treatment of Delayed Menstruation with Prostigmine: A Therapeutic Test for Early Pregnancy, J. A. M. A. **114**: 2090 (May 25) 1940.

12. Weiss, S., and Ellis, L. B.: Comparative Effects of Intravenous Administration to Man of Acetylcholine and Acetyl-Beta-Methyl-Choline, J. Pharmacol. & Exper. Therap. **52**: 113, 1934.

13. Hamilton, W. F.: The Patterns of the Arterial Pressure Pulse. Am. J. Physiol. **141**: 235, 1944.

14. Reynolds, S. R. M.: Physiology of the Uterus, New York, Paul B. Hoeber, Inc., 1939, p. 147.

and placenta. This increased uterine blood flow in the presence of a lowered arterial pressure can occur only when resistance within the uterine circulation is decreased. Prior to neostigmine administrations the maternal placental resistance was evidently high and maternal placental blood flow may have been adequately maintained only because the blood pressure was elevated. The fact that acetylcholine [15] and neostigmine [11] produce uterine hyperemia constitutes evidence to support the contention that neostigmine reduces the resistance within the uterine vascular bed. The cutaneous effects differ from those observed in normal and vasospastic patients in whom neostigmine increased the skin temperature and dilated small arteries but did not produce flushing.[16]

Neostigmine appeared to induce labor in these 8 patients who were pregnant seven, seven and one-half, eight, eight and one-quarter, eight and three-quarters, nine, nine and nine months. Uterine activity was normal and delivery was uncomplicated in 6 of the 8 patients, although 1 infant, seven months premature, died four hours post partum. In the other 2, who were multiparous eclamptic patients and who each received 1 mg. intramuscularly and 0.75 mg. intravenously, the uterus became hyperactive and cervical effacement and dilatation were delayed. Labor was dangerously prolonged to thirty-six and forty-eight hours. One of these

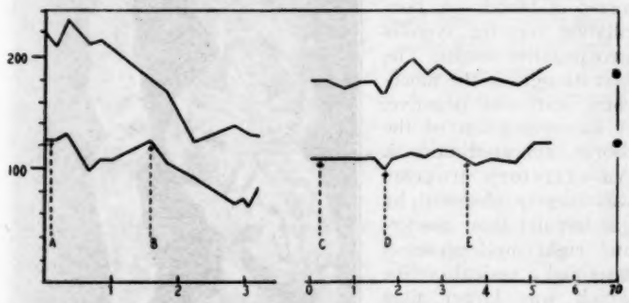

Fig. 2.—Plot of systolic and diastolic blood pressure of a preeclamptic patient who received neostigmine methylsulfate. Time indicated in intervals of one hour. At left, ante partum: At two hour intervals three intramuscular injections of 0.25 mg. of neostigmine methylsulfate were administered prior to *A*. The arterial pressure was increased 30 mm. of mercury during systole and 20 mm. of mercury during diastole. Two hours after the last intramuscular injection, an intravenous injection of 0.25 mg. of neostigmine methylsulfate was administered at *A*. Chill occurred and uterine contractions were initiated at *B*. The reduction of arterial pressure continued for four hours and then slowly rose as labor progressed. The baby was delivered nine hours after point *B*. At right, post partum: Seven hours after delivery at *C*, 0.5 mg. of neostigmine methylsulfate was administered intramuscularly. At *D* 0.25 mg. was administered intramuscularly. At *E* 0.25 mg. was administered intravenously. The arterial pressure was determined every half hour. No significant reduction was observed.

infants, seven and one-half months premature, died seventeen hours post partum. The death of these 2 infants can probably be ascribed to prematurity and the presence of toxemia. Neostigmine administrations probably were not a contributing factor. Used with caution and with proper allowance for its latent period, it may be less dangerous in some patients and no more dangerous in others than present medical methods of inducing labor. If used without discretion it would be expected to produce more detrimental effects than those observed with careless use of other methods.

The influence of neostigmine on convulsions of eclamptic patients has not been determined.

The observation that some preeclamptic gravid patients respond differently to neostigmine than normal gravid patients suggests that in preeclampsia (*a*) the tissues respond abnormally qualitatively or quantitatively to acetylcholine or, less likely, (*b*) the placenta and other tissues produce a slightly different choline derivative than is normally present.

15. Perlow, S.: Vasodilating Action of Prostigmine, J. Pharmacol. & Exper. Therap. **66**: 66, 1939.
16. Perlow, S.: Prostigmine in the Treatment of Peripheral Circulatory Disturbances, J. A. M. A. **114**: 1991 (May 18) 1940.

SUMMARY AND CONCLUSIONS

Individual susceptibility to neostigmine seemed to vary greatly, and even when administered intravenously a latent period of ninety to one hundred and twenty minutes was present. In all of the gravid patients it seemed to induce labor. In 2 of the patients in whom administrations were continued for twelve hours or longer the uterus became hyperreactive and hypertonic, resulting in a prolonged labor.

The presence of preeclampsia influences the type of response to moderate amounts of neostigmine. The drug does not lower the blood pressure of gravid patients unless they are preeclamptic. It does lower the arterial pressure of some but not all preeclamptic patients. The reduction in arterial pressure was always preceded or accompanied by chill, slight temperature elevation and initiation of labor. Preeclamptic patients have high resistance in the maternal placental vascular bed, and the reduction of blood pressure seems to be caused by decreased peripheral resistance in the uterine vascular bed. It seems to be accompanied by vasoconstriction of muscular, cutaneous and possibly renal vessels.

The observation that different preeclamptic patients may respond differently to moderate doses of neostigmine contributes additional support to the belief that there may be several different types of preeclampsia.

The cholinesterase activity of placentas from preeclamptic patients is greater than from normal patients.

ABSTRACT OF DISCUSSION

DR. A. R. ABARBANEL, Washington, D. C.: The work of Dr. Woodbury and his associates has apparently opened up a relatively new field in the possible treatment of toxemias of pregnancy. But, as they emphasize, neostigmine can be a double edged sword. They did mention that, but in 1 case the blood pressure did rise. That, of course, will depend on whether or not its action on the ganglion predominates over the peripheral action. The point that interested me in particular was the finding of a high cholinesterase in the toxemic placenta as compared to the normal. Cholinesterase is present in such superabundance in the tissues that it is hard to explain why there should be an actual increased amount in the placenta, except possibly that the placenta was putting out more acetylcholine in order to offset the toxic substance which was producing the unit of pathologic functioning, which most obstetricians now believe to be angiospasm. Whether this substance comes from the posterior pituitary, as many men, notably Dr. Hofbauer, believe is difficult to prove. There may be another factor in the increased cholinesterase, and that is the question of ions. We know that the cell is influenced by its ionic content and its ionic environment. It is quite possible that either a high calcium or a high potassium might have been a contributory factor. Early in pregnancy the uterus is relatively high in magnesium and low in calcium, but as term approaches the ratio of calcium and magnesium changes so that calcium becomes high, accounting for its increased irritability, and magnesium becomes low. Hyperirritability and hypertonicity of the uterus lead to many complications. One of the most severe of these is tetany of the uterus, in which we may get fetal anoxemia and eventual death or even actual rupture of the uterus. It is possible that in these 2 cases in which hyperirritability or hypertonicity was encountered atropine might have been effectual. There is another drug which is extremely effectual and which will abolish tetany of the uterus practically within thirty to sixty seconds. This drug is magnesium ion. Administered either as the sulfate or the gluconate intravenously, it prolongs the conduction rate

in the uterus so that it gives the uterus more of a restorative or recuperative phase following a muscular contraction. Magnesium will work against every type of oxytocic I have tried, including posterior pituitary injection, pitocin, pitressin, ergonovine, quinine and also when Bandl's ring contracture was encountered.

Dr. R. A. Woodbury, Augusta, Ga.: The suggestion made by Dr. Abarbanel that magnesium might be included with the treatment of neostigmine is excellent. We did not give these patients magnesium with neostigmine because it would have confused the story as to the action of the neostigmine, and yet it may well be that the administration of magnesium or some of the parasympatholytic drugs along with the neostigmine may remove the danger of the use of neostigmine in preeclamptic patients. It may protect the fetus from the hyperirritable uterus that neostigmine can produce.

Clinical Notes, Suggestions and New Instruments

COMPLETE URETERAL DUPLICATION TERMINATING IN THE SAME URETEROCELE AND RESULTING IN SEVERE HYDRONEPHROSIS

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and
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Of all the congenital abnormalities of the urinary tract, ureteroceles are among the most amenable to successful surgical treatment.

As reported by Thompson and Greene,[1] the majority of ureteroceles are congenital in origin, occur twice as frequently among women as they do among men, are most reliably diagnosed by cystoscopy and are best treated transurethrally by simple fulguration of the small ureteral orifice or a combination of ureteromeatotomy and fulguration of the walls of the ureterocele. These authors recognized that the presence of destroyed renal function or urinary calculi which could not be removed transurethrally necessitated open operation. While in the case that we are reporting there were features characteristic of moderate obstruction of the vesical neck, such as pronounced dysuria, a large atonic bladder, urographic evidence of a left nonfunctioning kidney and pyeloureterectasis of the other kidney and ureter, there have been numerous cases in which the ureterocele prolapsed through the urethra to cause intermittent complete urinary retention. Such a case was recently reported by Emmett and Logan.[2]

The case reported here presents several interesting features. First, it demonstrates how rapidly an obstructive lesion caused by a congenital ureterocele can result in severe hydronephrosis. Second, it is unique in that there was complete ureteral duplication with the two ureters opening into the same ureterocele. Finally, in this case a rather extensive surgical procedure was necessitated which was attended by a successful result.

REPORT OF CASE

A white girl aged 3½ years was brought to the Mayo Clinic in August 1944. A letter from the referring physician stated that the child, who had been the product of a full term normal spontaneous delivery and weighed 8½ pounds (3.8 Kg.) at birth, had first been taken ill with fever, urinary frequency, dysuria and pyuria at 11 months of age. A course of sulfanilamide therapy caused successful arrest of symptoms, though pyuria persisted. In the two years preceding this admission the child had suffered from several similar attacks, all responding symptomatically to sulfanilamide except for persistent pyuria, which frequently was grossly noticeable. Three days before admission to the clinic the patient had a severe attack with elevated temperature and dysuria, which was so intense that it caused the patient to avoid micturition even though the bladder was apparently overdistended.

A review of systems made by questioning the patient's mother gave negative results. The patient was the only child of two healthy parents. The past medical history was negative except for an attack of infantile eczema, which had been absent for the past year. The child's developmental history was entirely normal.

Physical examination revealed that the child was well developed but obviously acutely ill. The patient's oral temperature was 102.8 F. The pulse rate was 120 per minute. The respiratory rate was 28 per minute. The results of laboratory analyses were as follows: Erythrocytes in the urine were graded 1 and leukocytes were graded 3 (on the basis of 1 to 4, in which 1 represents the smallest and 4 the largest number of formed elements). Staphylococcus aureus and Streptococcus fecalis were cultured from the urine. The concentration of urea was 26 mg. and that of hemoglobin was 10.6 Gm. per hundred cubic centimeters of blood. Erythrocytes numbered 3,620,000 and leukocytes numbered 9,600 in each cubic millimeter of blood. A flocculation test for syphilis gave negative results. The first strength of the tuberculin test was negative. A roentgenogram of the thorax appeared normal. An excretory urogram was largely obscured by gas but did show moderate right pyeloureterectasis and a vesical outline which was larger than normal. Accurate evaluation of the left kidney and ureter was impossible because of greatly reduced function, with only questionable visualization of the upper calix.

Double ureter and hydronephrotic kidney with only thin shell of atrophic renal cortex remaining. Both ureters are much dilated and terminate within the same small segment of ureterocele.

On cystoscopy performed with the patient under ether and nitrous oxide anesthesia, a large volume of urine was found in the bladder, which was greatly distended and slightly trabeculated. Neither ureteral orifice could be seen. In the region of the left ureteral orifice was a large soft structure which the cystoscopist believed probably represented a ureterocele and which he thought might be producing obstruction at the vesical neck. Because the exact nature of abnormality within the bladder could not be accurately determined cystoscopically and because the function of the left kidney seemed to have been destroyed, suprapubic exploration was advised.

With the patient under ether and nitrous oxide anesthesia, and through a primary low midline incision, the bladder was opened. It appeared greatly enlarged and was the seat of a moderate amount of inflammation. The left side of the bladder was occupied by a large ureterocele and it was found to contain two ureteral orifices. The right ureteral orifice appeared to be normal. On transvesical excision of the ureterocele it was apparent that one orifice led into a much dilated ureter while the other orifice led into a large pocket, which on further exploration proved to be a hydroureter. The original incision

From the Division of Surgery, Mayo Clinic (Dr. Counseller).

1. Thompson, G. J., and Greene, L. F.: Ureterocele: A Clinical Study and a Report of 37 Cases, J. Urol. **47**: 800-809 (June) 1942.
2. Emmett, J. L., and Logan, G. B.: Ureterocele with Prolapse Through the Urethra, J. Urol. **51**: 19-23 (Jan.) 1944.

was extended transperitoneally and both of these dilated ureters were found to join a hydronephrotic left kidney in which more than 90 per cent of the renal substance had been destroyed. Both dilated ureters as well as the hydronephrotic left kidney were removed transperitoneally. The right kidney was found to be normal and had a normal ureterovesical opening. One small 18 F. bivalved catheter was inserted into the bladder as a cystostomy tube and a 4 F. ureteral catheter was left in the right ureter with its upper end in the renal pelvis and its lower end extending through the urethra. The peritoneum was closed after 5 Gm. of sulfanilamide had been left in the peritoneal cavity; 2.5 Gm. of sulfanilamide was left in the incision, which was closed with double continuous number 1 chromic catgut with single interrupted chromic sutures in the fascia. A split rubber tube was left in the incision. The patient was given a transfusion of 250 cc. of compatible blood at the completion of the operation.

The removed specimen consisted of a kidney, double ureter and a portion of the bladder. The kidney was considerably hydronephrotic, with almost complete destruction of the renal substance. One ureter, believed to be the functional one, was dilated throughout with a diameter slightly more than 1 cm. Parallel to the ureter was another one measuring approximately 25 cm. in length and approximately 4 cm. in diameter.

The split rubber tube was removed on the second day after operation. The ureteral catheter was withdrawn from the right ureter on the fourth postoperative day. The cystostomy tube was removed on the fifteenth day and thereafter the suprapubic fistula remained dry and healed rapidly. The patient was dismissed from the hospital on the twenty-third postoperative day. At this time the dysuria was reduced by more than 50 per cent but Streptococcus fecalis was cultured from the urine. The patient was dismissed with instructions to receive alternate courses of sulfathiazole and a mandelic acid preparation. She was taken home to the care of her home physician, who sent her back to us one month later for a routine follow-up visit. Examination at the time disclosed that the patient appeared and felt perfectly well. Streptococcus fecalis was again cultured from the urine, which now appeared to be crystal clear. A further course of mandelic acid therapy was prescribed for the patient.

The patient was reexamined in January 1945. Her parents volunteered the information that she was enjoying perfect health and was voiding normally. No residual urine was present in the bladder. An excretory urogram revealed that the right kidney was functioning well with minimal pyelocaliectasis. The vesical outline appeared normal. Because Streptococcus fecalis was still present in the urine, mandelic acid therapy was continued.

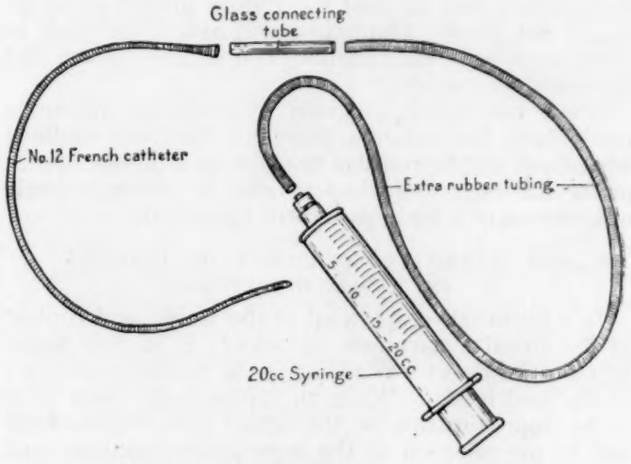
RECTAL INSTILLATION OF AMINOPHYLLINE IN INTRACTABLE ASTHMA

ALVAN L. BARACH, M.D., NEW YORK

Intravenous injection of aminophylline in patients with intractable asthma has become recognized as an exceedingly valuable therapeutic remedy following its introduction in 1937.[1] Since termination of bronchial spasm has been satisfactorily accomplished in more than 200 patients by rectal instillation of this drug, it has been repeatedly employed by nurses and by patients themselves in a program of bronchial relaxation.[2] The relief of bronchial spasm takes place in ten to thirty minutes, more gradually than with intravenous injection, but the side effects on the circulation, such as dizziness and faintness, are rarely encountered and have in no instance been troublesome. Nausea and vomiting may take place after large doses, as in intravenous injection, but are much less apt to occur if the patient is in the reclining position for one hour after its administration. The intravenous ampule of 20 cc. containing 0.48 Gm. of the drug has been employed, but it is much less expensive to use powders of 0.5, 0.6 or 0.7 Gm., dissolved at the time of administration in 20 cc. of tap water. There is admittedly less uniformity in absorption from the rectum than from the intravenous injection, but the availability of the method to the patient outweighs this relatively minor disadvantage.

The apparatus consists of a 20 cc. glass syringe, a No. 12 French rubber catheter and a connecting rubber tube attached to the open end of the catheter, approximately 18 inches in length and ⅛ inch in diameter.

At the time of treatment a powder of 0.6 Gm. is dissolved in 20 cc. of tap water and drawn into the glass syringe. The syringe is placed on the bedside table prior to introduction of the rubber catheter. Lubrication of both the anal mucosa and the rubber catheter is important to prevent irritation from long continued use. The catheter is then easily inserted into



Apparatus for rectal instillation of aminophylline.

the rectum for a distance of 2 or 3 inches; the rubber tube connection is brought forward in front of the patient, the syringe attached and the aminophylline delivered into the rectum. The catheter is then pinched tightly, to prevent drops of the solution from wetting the bed, and withdrawn. Other advantages of the method are that (1) the anal canal is not dilated by a large enema tube, (2) there is a minimal introduction of air, which may take place with the use of a tube and funnel, and (3) there is no irritation whatever if properly employed.

Although aminophylline is by far the most valuable drug in restoring sensitiveness to epinephrine, it must be borne in mind that patients will at times become refractory to aminophylline also. The treatment of this unfortunate complication is beyond the scope of the present paper, but it may be pointed out that the drug must then be discontinued and recourse had to other methods of bronchial relaxation, such as helium-oxygen therapy or colonic ether, in order to restore the patient's responsiveness to aminophylline.

SUMMARY

Rectal instillation of aminophylline by means of a No. 12 French catheter, a rubber tube connection and a 20 cc. glass syringe has certain advantages over intravenous injection in the treatment of intractable asthma. The procedure has been carried out by nurses, relatives and patients themselves without delay or difficulty. Circulatory side-effects of rapid intravenous injection, such as dizziness and faintness, were rarely encountered and never troublesome.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.

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Council on Foods and Nutrition

SPECIAL ARTICLE

This is the eighth of a series of articles discussing the significance of protein nutrition in health and disease. This material was prepared by the authors at the request of the Council and has been authorized for publication.

GEORGE K. ANDERSON, M.D., *Secretary.*

SELECTION OF PROTEIN CONTAINING FOODS TO MEET PROTEIN REQUIREMENTS

DOROTHEA F. TURNER, S.M.
CHICAGO

In planning a dietary regimen appropriate in protein content for different health and socioeconomic conditions, several factors must be considered. Some evaluation must be made of the nutritive efficiency of proteins in a mixed dietary; selections must be made of the proper kind and amount of protein containing foods which may be used for various dietary prescriptions; and, finally, adaptations will have to be made to correspond with the patient's food habits, income and rationing allowances.

Space has not been given to itemizing numerous meal plans, but rather a procedure has been outlined whereby it will be possible to make up a dietary appropriate for each individual patient by making simple adaptations of a basic pattern of food intake.

THE NUTRITIVE EFFICIENCY OF PROTEINS IN A MIXED DIETARY

Is a quantitative appraisal of the amino acid content of the mixed dietary now in order? If so, this would be the most direct way to assess the nutritive efficiency of the food intake. While an approach has been made to an approximation of the amino acid requirements and to the selection of the appropriate quantities and combinations of food proteins which will meet these needs, the dietitian is not as yet adequately prepared to calculate accurately the amino acid content of the diet. As Block and Bolling [1] have stated, "It should be recognized that the methods used for estimating amino acids are not of equal precision. Errors are introduced by the formation of inhibiting substances or the partial destruction or modification of certain amino acids during hydrolysis. Mechanical and solubility losses also play a part." Nevertheless, present methods are of special use in comparative investigations and, if employed in conjunction with biologic experiments, are of value in suggesting the nutritional evaluation of proteins and the choosing of proteins which will be mutually supplementary.

The various methods of determining the relative values indicate that proteins of animal origin, i. e. milk, eggs, meat, poultry, fish and cheese, are superior in nutritive efficiency to most vegetable proteins. Furthermore, while these animal proteins are much alike in the value of their proteins, the same is not true of the vegetable proteins.[2] Thus, oats rank higher in biologic value than white wheat flour, but wheat is superior to corn in biologic value. Although beans, peas and lentils are considered of rather low biologic value, Everson and Heckert [3] have found that heating for forty-five minutes at 15 pounds pressure improved the nutritive value of mature soybeans, pinto beans, navy beans and kidney beans. Two varieties of peas were lowered in biologic value by the heating. In contrast, immature unheated peas appeared to supply an unusually high grade of protein. Peanuts rank high in biologic value. White wheat flour has been found to be decidedly lower in nutritive efficiency than the whole grain. Chick [4] has investigated the nutritive efficiency of the protein in three flours, from the same sample of grain, representing the 100 per cent whole grain, 85 per cent extractions and 75 per cent extraction. The third flour was that used for making ordinary white bread. The superior biologic value of the protein of the 100 per cent whole grain was striking and conclusive.

In spite of the lower biologic value of legumes and grains, it is well known that, when combined together in the diet, mutually supplementary relationships exist. Furthermore, it is recognized that a relatively small amount of animal protein will enhance considerably the value of the grains and legumes.[5]

From a practical point of view a quantitative evaluation of the supplementary relationship of proteins of mixed dietaries is needed. However, comparatively little is known about the biologic value of proteins making up a mixed diet. Recently Macrae, Henry and Kon [6] reported a study of the biologic value of mixed proteins in food served in Royal Air Force stations in England. The protein consumed per man daily varied from 83 to 101 Gm., and the proportion of the protein which was animal in origin ranged from 42 to 45 per cent. The results revealed that the diets had a high biologic value and a high degree of digestibility.

While more research is needed on the biologic value of the whole diet, it would appear that the current dietetic practice, that of providing one half of the protein from animal sources,[7] will insure a satisfactory factor of safety for the levels of protein intake recommended by the Food and Nutrition Board of the National Research Council [8] for the adult maintenance diet. In therapeutic diets, and in diets in which growth is a factor, it is a common practice to provide one half to two thirds of the protein from animal sources.

THE ORGANIZATION OF PROTEIN CONTAINING FOODS INTO PATTERNS OF FOOD INTAKE

The actual combining of protein containing foods into patterns of food intake may be organized most simply by noting the relative amounts of protein contributed by various food groups in a basic dietary pattern. From this basic plan it will then be possible to make adaptations in the protein intake suitable for various dietary prescriptions. An example of such a basic plan is presented in table 1.

From the Nutrition Clinic, University of Chicago Clinics.

1. Block, R. J., and Bolling, Diana: Nutritional Opportunities with Amino Acids, J. Am. Dietet. A. **20:** 69-76 (Feb.) 1944.
2. Beach, E. F.; Munks, Bertha; Robinson, Abner, and Macy, Icie G.: Dietary Evaluation of Animal Proteins from Their Amino Acid Contents, J. Am. Dietet. A. **19:** 570-575 (Aug.) 1943. Maynard, L. A.: Foods of Plant Origin, Handbook of Nutrition, Chicago, American Medical Association, 1943, pp. 241-257.
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4. Chick, Harriette: Biological Value of the Proteins Contained in Wheat Flours, Lancet **1:** 405 (April 4) 1942.
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6. Macrae, T. F.; Henry, K. M., and Kon, S. K.: The Biological Value of Mixed Proteins in Food Served in Royal Air Force Airmen's Messes, Biochem. J. **37:** 225-230 (July) 1943.
7. Bogert, L. J., and Porter, M. T.: Dietetics Simplified, New York. Macmillan Company, 1940, pp. 33-48. Clayton, Mary M.: Protein in the Low Cost Diet, J. Am. Dietet. A. **18:** 462 (July) 1942.
8. Food and Nutrition Board, National Research Council: Recommended Dietary Allowances, Handbook of Nutrition, Chicago, American Medical Association, 1943, pp. 333-338.

This basic pattern of food intake might be outlined in innumerable meal plans. Two examples of possible combinations of these foods which would give the approximate protein intake listed in table 1 are given in table 2.

The basic pattern of food intake supplies approximately 60 per cent of the protein from animal sources and approximates also the recommended dietary allowances for minerals and vitamins outlined by the Food and Nutrition Board of the National Research Council.[8]

In addition to the valuable amounts of protein supplied by these foods, other nutrients are present which in some respects differ either in kind or in relative amount. For example, the milk contributes the major portion of calcium and phosphorus in the diet as well as the vitamins of the B complex. While 2½ ounces of cottage cheese would be an equivalent protein substitute for 1 pint of milk, the cottage cheese [9] would supply less than one tenth of the calcium, phosphorus, iron, vitamin A, thiamine and riboflavin supplied by the milk. Two and one-half ounces of American Cheddar cheese [9] would supply calcium equivalent to 1 pint of milk but would be much lower in the vitamins of the B complex. In this case the addition of liver or other glandular meat one or two times a week would be desirable to augment the iron, vitamin A and B vitamins in the diet; pork would enrich the thiamine intake. Eggs will supply a significant amount of vitamin A and iron. Legumes and whole grains will also contribute iron and vitamins of the B complex. Table 3 is a comparative table of nutrients in some of the protein containing foods.

TABLE 1.—*Basic Pattern of Daily Food Intake for an Adult Man (70 Kg.)*

Daily Food Intake	Approximation of Protein Content,* Gm.
16 oz. (1 pint) of fluid milk or 8 oz. of evaporated milk or 1½ oz. (5 tablespoons) of dried skim milk..... (1 serving [4 oz.] of milk pudding or ice cream may be approximately equivalent to 3 oz. of fluid milk)	15
3 oz. serving of meat or poultry or fish (cooked, edible portion) or 1½ oz. of soybean flour or 5 oz. (¾ cup) of cooked soybeans.....	18
1 oz. of American cheddar type cheese or 1 oz. of cottage cheese or 1 egg.....	6
3 oz. serving (one half cup) of cooked peas, navy beans, or lima beans, or ¼ cup cooked soybeans, or ⅔ oz. (1½ level tablespoons) of peanut butter.....	6
3 oz. serving (⅓ cup) of potatoes.....	2
Other vegetable—3 servings, of which 1 is green leafy or yellow	3
Fruits—2 servings, of which 1 is citrus or tomato.....	2
Six slices of bread, enriched or whole grain, or equivalent grain product ..... (The approximte protein equivalent of one slice of bread is a 1 oz. (dry weight) serving of cereal or ½ cup of cooked spaghetti or noodles or 6 soda crackers or 1 small piece of cake or a 2 inch cube of cornbread or 3 graham crackers)	18
Total.....	70

* Meat, poultry, fish, cheese and nuts range between 10 and 30 per cent protein. Grain products (dry weight), fresh peas and beans contain between 7 and 15 per cent protein. Eggs contain approximately 12 per cent protein. Milk is about 3 per cent protein. For more detailed figures on the percentage composition of protein in foods see Chatfield, C., and Adams, G.: Proximate Composition of American Food Materials, Circular No. 549, U. S. Dept. of Agric., June 1940.

9. Cheese may be roughly divided into two classes, one in which the curd is formed through the action of the enzyme rennet, the other in which the curd is formed through the action of lactic acid. When the curd is formed through the action of rennet, as in American Cheddar cheese, the calcium is retained in the curd. When lactic acid is used to produce the curd, as in cottage cheese, the calcium is lost in the whey.

ADAPTATIONS OF THE BASIC PATTERN

Considerable elasticity is possible in the selection of protein foods from the basic pattern. From this basic plan, adaptations can be made suitable for the diet for the normal adult woman and the diet for pregnancy and lactation, for the needs of children and for high protein diets. Innumerable combinations of the foods on the basic plan are possible in making up satisfactory outlines for meals. However, only a few examples follow, since a specific dietary prescription will need to be integrated with the individual patient's food habits and his social and economic problems.

TABLE 2.—*Combinations of Foods Embodying Basic Pattern*

Breakfast	Noon Meal	Evening Meal
Citrus fruit 1 egg 2 slices of toast Coffee with milk or cream	Sandwich (peanut butter or cheese or meat) Vegetable salad 1 glass milk Fruit Cake	Meat Potato Cooked vegetable Mixed green vegetable salad 1 glass milk 1 slice bread Ice cream
	or	
Banana Whole grain cereal with milk 1 slice toast Coffee with milk or cream	Baked navy beans with pork Cabbage salad 1 glass milk Fruit custard 1 slice bread	Soup with crackers Chicken Sweet potato Cooked greens Grapefruit and orange salad Ice cream Cake 1 slice bread

Diet for the Adult Woman.—If 1 Gm. of protein per kilogram of body weight is used as a guide in setting up the level of protein in the diet, the dietary prescription may range between 50 and 75 Gm. of protein daily. A sample plan containing 50 Gm. of protein is given in table 4. Again, if less than 1 pint of milk is used in the dietary plan, it will be necessary to make an effort to replace not only the protein but also the calcium, phosphorus and vitamins of the B complex which milk supplies in major amounts.

TABLE 3.—*Nutrients in Certain Protein Containing Foods* *

Amount of Food	Protein, Gm.	Minerals: Calcium, Gm.	Minerals: Iron, Mg.	Vitamins: Vitamin A, I. U.	Vitamins: Thiamine, Mg.	Vitamins: Riboflavin, Mg.	Vitamins: Niacin, Mg.
Milk, 1 pint.....	15	0.60	1.0	850	0.20	0.90	0.55
Cheese, cottage, 2½ oz. ...	15	0.06	0.1	(50)†	(0.01)†	(0.10)†	
Cheese, American cheddar, 2½ oz.	15	0.65	0.8	1,070	0.03	0.36	0.02
Beef, roast, 3 oz.	18	0.01	2.6		0.05	0.18	3.62
Pork, roast, 3 oz.	18	0.01	2.5		0.60	0.24	3.07
Liver, fried, 3 oz.	18	0.01	8.2	27,500	0.27	2.16	12.07
Peanut butter, ⅔ oz.	6	0.01	0.4		0.04	0.02	3.20
Navy beans, cooked, 3 oz..	6	0.04	2.5		0.10	0.08	0.50
Soybean flour, ½ oz.	6	0.05	2.0		0.09	0.06	0.60
Whole wheat bread, 2 oz. (2 slices).....	6	0.04	1.6		0.18	0.08	2.10
Egg, one.....	6	0.02	1.3	450	0.07	0.18	0.03

* Tables of Food Composition Giving Proximate, Mineral and Vitamin Components of Foods, Committee on Food Composition of the Food and Nutrition Board, National Research Council March 1, 1944; Tables of Vitamin Losses in Cooking of Foods, June 1, 1944.
† ( ) Imputed values.

Diet for Pregnancy and Lactation.—Between 85 and 125 Gm. of protein may be recommended during this period, two thirds of which can easily be provided as animal protein. Extra needs for calcium, phosphorus, iron and vitamins have been indicated in the recommended dietary allowances of the Food and Nutrition Board of the National Research Council.[8] These extra needs can be supplied to excellent advantage simply by

adding milk to the basic pattern of food intake. Skim milk (defatted milk solids) or buttermilk may be used. When the patient is not accustomed to drinking milk, it may be desirable to provide suggestions for the use of milk in soups, desserts or flavored beverages. The most inconspicuous and, in many cases, the most acceptable way in which to add milk is in the form of dried milk. Approximately 1½ ounces (5 tablespoons) of dried skim milk (defatted milk solids) will equal

TABLE 4.—*Sample Plan Containing 50 Gm. of Protein*

	Protein, Gm.
1 pint of milk or milk equivalent	15
1 egg	6
2 ounces meat or poultry or fish	12
3 vegetables	3
2 fruits	2
4 slices of bread or equivalent grain product	12
Total	50

1 pint of fluid milk. This dried milk may be incorporated as a dry ingredient in the preparation of meat loaf, mashed potatoes, sandwich spreads, cooked cereals, hot breads, cookies, pastries or puddings with little difficulty. Also a palatable drink may be prepared by adding approximately 2½ tablespoons of dried skim milk to 1 glass (8 ounces) of fluid milk. This will provide approximately 15 Gm. of high quality protein per glass. In some parts of the country, dried milk may be obtained from the retail grocery store. In other places it may be necessary to depend on the courtesy of a bakery shop or hospital, or dairy.

Where cheese is substituted for milk, due attention must again be given in order to compensate for the large decrease in minerals and vitamins which would otherwise result. In this case the increased use of glandular meats and pork will be useful in augmenting these nutrients. Where milk or American Cheddar type cheese is not tolerated it is unlikely that the calcium and phosphorus will be met with other foods. Further attention will then have to be given to compensate satisfactorily for the protein and for other nutrients provided in milk. An example of a diet containing 100 Gm. of protein and meeting the recommended allowances of the Food and Nutrition Board of the National Research Council [8] for minerals and vitamins during lactation is presented in table 5.

Diet for Children.—Relatively more protein is recommended per unit of weight during the growth period. Recommended daily allowances vary between 40 and 100 Gm. of protein daily, depending on the age and "ideal" size of the child. The actual food selection will be similar to that outlined in the basic pattern of food intake, but the relative amounts of each food will vary during the child's developmental period. In younger children the 30 Gm. of protein provided in 1 quart of milk will insure a surplus of animal protein. With an egg daily and a small serving (2 ounces) of meat or cheese in addition, it will be possible to provide two thirds of the protein as animal protein on levels up to 65 Gm. of protein daily. When levels of 100 Gm. of protein daily for adolescent children are to be provided, a plan similar to the one suggested for pregnancy and lactation will supply the high levels of minerals and vitamins needed.

High Protein Diets.—When it is desirable to increase the protein content of the diet to levels as high as 150 Gm. daily, it may be difficult from the patient's point of view to increase further the protein containing foods enumerated on the basic pattern of food intake. The patient may have objections to the bulk, to the cost or to the flavor of these foods. In this case, use may be made of concentrated food sources of protein, particularly dried milk, which contains 25 per cent protein in dried whole milk and 35 per cent protein in defatted milk solids (dried skim milk). Other protein rich foods may be used, such as soybean flour, which ranges between 37 and 45 per cent protein, peanut flour, which may be 50 to 60 per cent protein, or dried yeast, which is approximately 45 per cent protein. Corn germ and wheat germ also have possibilities for use as valuable protein foods. Plain, dried gelatin contains 85 per cent protein.

As already mentioned, dried milk is one of the concentrated food sources of protein which may be used the most successfully. It may readily be incorporated as a dry ingredient in hot breads, cookies, cake, sandwich spreads, mashed potatoes, meat loaf, milk beverages and desserts, hot cereals and cream sauces, resulting in a decided increase in the protein intake. As stated previously, 2½ tablespoons of dried skim milk may be added to one glass (8 ounces) of fluid milk, thus providing 15 Gm. of high quality protein per glass of milk. This is a low cost product which supplies excellent quality proteins.

Soybean flour is another mild flavored, low cost product which can be successfully incorporated in cooking. Tabulations of comparative digestibility coefficients, amino acid analyses and results of growth promoting animal feeding tests all contribute to the conclusion that the protein of the soybean is of high biologic value. Soybean products are generally available at the present time and can be used in such prepared foods as pancake and muffin mixes, cereal products, macaroni and other paste goods, meat products, soups, breads and pastry products.[10] Approximately 500 tested recipes in both large quantity and family size have been collected from various agencies by the Diet Therapy Section of the American Dietetic Association.[11]

Since the production of peanut flour has increased as the result of priority allowances by the War Production

TABLE 5.—*Diet Containing 100 Gm. of Protein*

Daily Food Intake	Protein, Gm.
40 oz. fluid milk	36
2 eggs	12
3 oz. serving of meat, poultry or fish	18
1 oz. American cheddar cheese, or 7 oz. milk	6
3 oz. serving of legumes or 1½ tablespoons peanut butter	6
1 serving of potatoes	2
3 servings of vegetables	3
2 servings of citrus fruit or tomato	2
5 slices bread, whole grain or enriched	15
Total	100

Board, the use of this product is appropriate at this time.[12] As peanut flour contains approximately 50 to 60 per cent protein, an effective increase can be made in the protein intake with this product. It may be blended with cereals such as wheat, cornmeal, hominy grits, rolled oats, farina and various prepared dry cereals to increase their food value, and with cereal flour used in baked products. It can also be used as an extender and binder in meat loaves, sausage and

10. Leaming, Betty G.: Soya Products—Availability, Nutritional Values, and Utilization, J. Am. Dietet. A. **19**: 824-827 (Dec.) 1943.
11. Note: Soya Products, J. Am. Dietet. A. **20**: 307 (May) 1944.
12. Peanut Flour, editorial, J. Am. Dietet. A. **19**: 640-642 (Sept.) 1943.

other meat products and as a base in dry soup concentrates.[13]

Another low cost product which has considerable merit is dried brewers' yeast, which contains approximately 45 per cent protein. The advantages of yeast, have been appreciated not only because it is an inexpensive source of recognized vitamins and protein but also because many experiments indicate that it contains essential factors that have not been isolated and recognized. Yeast makes pleasing combinations with syrup or peanut butter. It can also be used in baked products such as bread, cookies and doughnuts. Heller, McCay and Lyon [14] incorporated significant amounts of yeast successfully in meat loaves, stews, cheese dishes, baked beans and meat balls. These products were all accepted favorably in an industrial cafeteria serving 1,500 people daily. Carr [15] has published recipes for the use of yeast in home cookery.

Use may also be made of wheat germ which contains approximately 35 per cent good quality protein. It may be added directly to meat dishes, sandwich mixes, soups, cereal dishes or fruit mixtures. It has not been incorporated successfully in significant amounts in breads or cakes because of the change made in the texture of the baked product. Corn germ, another vegetable product with possibilities for becoming a valuable protein food, contains 20 per cent protein of a quality comparable to milk, meat and soybean protein.

Commercial products are available which combine dried milk, dried egg, wheat germ, whole grains and synthetic vitamins. Certain of these may be incorporated in milk beverages, thus being of especial value when liquid or soft diets are recommended. Bauman [17] has suggested a formula for a high protein beverage to increase the protein intake. Gelatin also may be incorporated in significant amounts in hot beverages or soups.

OTHER CONSIDERATIONS

In order to make the dietary plan acceptable to the patient it will be necessary to take into consideration the economic factors, the social and emotional problems of the individual patient and nowadays the rationing of foods.

An appraisal of protein containing foods in terms of cost usually shows that meat, poultry and fish are the most expensive items in the menu. While the current ceiling prices have a leveling effect on price at the present time, the usual factors of cost of production and marketing still need to be considered. The relative importance of these factors will vary in different parts of the country. Thus, if fish or poultry is more readily available they can be used, since these foods are of equal protein value with meat. At the present time the more select cuts of meat are scarce. More of the range fed, utility grade beef is available for civilian use. The utility grade beef contains less fat and a slightly higher percentage of protein than the choice cuts. Thus, on the basis of nutritive value no discrimination need be made against the lower grade meats or the less popular cuts. These meats are less tender, however. Tenderness may be obtained by a somewhat longer cooking period with moist heat, which brings about a hydrolysis of the collagen in the connective tissue to gelatin. To effect the greatest economy in both money and rationing allowances, it may be necessary to recommend to the patient that he (1) buy kinds and cuts of meats not used before, as less tender cuts and organ meats, (2) learn the suitable preparation for each cut, using low temperature cooking for all methods, (3) extend the flavor of meat with bland foods such as spaghetti, noodles and corn meal, (4) select recipes which combine the best elements of appetite appeal with nutritive value and (5) avoid kitchen waste, table waste and waste from improper storage. Furthermore, it is not necessary to use large amounts of meat even in the high protein diet.[18] Adequate substitutions may be made for meat by the selection of equivalent amounts of other protein containing foods. Thus the equivalent of 1 ounce of meat might be 1 ounce of poultry or fish, or 1 egg, or 1 glass of milk, or 1½ tablespoons of peanut butter or 1 serving of legumes. In addition such low cost, unrationed products which are concentrated sources of protein may be used advantageously as dried milk, soya products, peanut flour, dried brewers' yeast and wheat or corn germ. At the present time it is not difficult to obtain adequate amounts of protein containing foods from the unrationed list.

Among the less expensive protein containing foods, milk is the most important not only in terms of good quality protein but in terms of other nutrients as well. Furthermore, the valuable supplementary protein relationships between milk and vegetable proteins will enable the patient to make greater use of the low cost legume and grain proteins with safety.

The patient's acceptance of protein foods to which he has not been accustomed will depend on satisfactory adaptations of the dietary plan to the different national, regional, religious or racial backgrounds of each patient.[19] Furthermore, the instructions of the food clinician become increasingly effective as psychologic factors are taken into account in teaching nutrition. Behavior in relation to food is often an interplay between the physical and the emotional life. As in other phases of medicine, the patient must be considered as a "whole" if the therapy is to be effective.

13. A booklet containing recipes for the use of this flour may be obtained from the National Peanut Council, Inc., Atlanta, Ga.
14. Heller, Christene A.; McCay, C. M., and Lyon, C. B.: Adequacy of the Industrial Lunch and the Use of Brewers' Yeast as a Supplement, J. Nutrition **26**: 385-390 (Oct.) 1943.
15. Carr, R. E.: Vitamin Rich Baked Products, Michigan State Bull. 178, 1941.
16. Corn Germ, a Valuable Protein Food, Nutrition Rev. **2**: 212-213 (July) 1944.
17. Bauman, Louis: A High Protein Beverage, J. A. M. A. **121**: 1283 (April 17) 1943.
18. Johnson, Doris: High-Protein Diets, J. Am. Dietet. A. **20**: 666-667 (Nov.) 1944.
19. Report of the Committee on Food Habits 1941-1943: The Problem of Changing Food Habits, Bulletin of the National Research Council, No. 108, October 1943.

ACCEPTED FOODS

The following additional foods have been accepted as conforming to the Rules of the Council on Foods and Nutrition of the American Medical Association for admission to Accepted Foods.

GEORGE K. ANDERSON, M.D., *Secretary.*

PREPARATIONS USED IN THE FEEDING OF INFANTS (*See* Accepted Foods, 1939, p. 156)

Beech-Nut Packing Company, Canajoharie, N. Y.

BEECH-NUT STRAINED PEACHES WITH LEMON JUICE.

Analysis (submitted by manufacturer).—Total solids 15.66%, moisture 84.34%, ash 0.44%, fat (ether extract) 0.20%, protein (N × 6.25) 0.69%, crude fiber 0.24%, carbohydrates (other than crude fiber) 13.91%, calcium (Ca) 0.027%, phosphorus (P) 0.026%, iron total 0.68 mg. per hundred grams, iron "available" (Bipyridyl method) 0.40 mg. per hundred grams, copper (Cu) 0.11 mg. per hundred grams.

Calories.—60 per hundred grams, 17 per ounce.

Vitamins.—Vitamin A .....350 U. S. P. units per hundred grams
Thiamine .....0.015 mg. per hundred grams
Riboflavin .....0.012 mg. per hundred grams
Niacin .....0.63 mg. per hundred grams
Ascorbic acid .....3.3 mg. per hundred grams

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SATURDAY, JUNE 23, 1945

ENZYMIC DETOXICATION OF POISON IVY

During recent years Hill,[1] Mason [2] and others have isolated and identified certain skin irritants from poison ivy, poison oak and related plants. Keil [3] has shown that these substances are phenols or catechols characterized by long unsaturated side chains attached to the phenolic ring. The toxic properties are in large part due to the presence of OH groups in this ring. On exposure to air a slow auto-oxidation of these toxic groups takes place. This has suggested that a logical method of preventing or treating poison ivy dermatitis would be by the use of strong oxidents such as ferric chloride and potassium permanganate.

In their search for a less irritating therapeutic agent, Sizer and Prokesch [4] of the Massachusetts Institute of Technology tested whether or not a similar oxidative detoxication can be effected by the use of enzymes. Since phenolic oxidases are not highly specific,[5] Sizer selected mushroom tyrosinase for his oxidation tests. The isolated toxic principle of poison ivy was mixed with tyrosinase and the rate of oxidation determined by measuring the rate of oxygen consumption in the Barcroft respirometer. The mixture consisted of 1 cc. of poison ivy extract, 0.1 cc. of tyrosinase and 3.2 cc. of buffer (p_H 7.3). The consumption of oxygen proceeded rapidly to 60 per cent completeness during the first four hours and with increasing slowness for five days, when the oxidation was practically complete. Additional evidence that the toxic molecules had undergone catalytic oxidation was furnished by a gradual darkening of the color of the mixture.

The dermatitis producing properties were greatly reduced. This was shown by parallel patch tests on both human and sensitized [6] guinea pig skin. In all cases a much more severe dermatitis was noted in the control area covered with the untreated toxin than in the area covered with the oxidized toxin. In many cases dermatitis was not noted with the oxidized product.

The therapeutic efficiency of tyrosinase was tested by applying simultaneously to human skin a poison ivy concentrate and tyrosinase, control test being made with boiled or inactivated tyrosinase. In all cases the area treated with the active enzyme gave much less dermatitis than the control, indicating sufficiently rapid oxidation to be of therapeutic promise. If equally successful results can be obtained by applying tyrosinase some time after the toxicant has reached the skin or, preferably, after erythema has developed, then a new method of treating poison ivy dermatitis will be available. Clinical tests of the latter possibilities are now in progress.

1. Hill, G. A.; Mattacotti, V., and Graham, W. D.: J. Am. Chem. Soc. **56**: 2736, 1934.
2. Mason, H. S., and Schwartz, L.: J. Am. Chem. Soc. **64**: 3058, 1942.
3. Keil, H.; Wasserman, D., and Dawson, C. R.: J. Exper. Med. **80**: 275, 1944.
4. Sizer, I. W., and Prokesch, C. E.: Science **101**: 517 (May 18) 1945.
5. Nelson, J. M., and Dawson, C. R.: Advances Enzymol. **4**: 99, 1944.
6. Simon, F. A.: J. Immunol. **30**: 275, 1936.

NUTRITION AND CANCER

The nutritional state of the patient assumes an important role in curing disease. In both experimental and spontaneous tumors the influence of energy intake, fat consumption per se, protein content of the diet and deficiency of certain vitamins have been shown to influence the course of development of the tumor. Many investigations have shown that mere restriction of food consumption in animals will reduce the incidence of both spontaneous and artificially induced tumors. Tannenbaum [1] has demonstrated with statistics gathered from the life insurance companies that an increased incidence of cancer occurs among persons who were overweight at the time the insurance policy was issued. On the basis of such evidence Potter [2] has even advocated ample exercise and a minimum food consumption as a measure for the prevention of human cancer.

Recently Morris [3] has shown that in mice on a restricted calory regimen, so that the weanlings did not gain weight and adult animals lost up to 45 per cent of their weight, the incidence of spontaneous mammary tumors was reduced from a control value of 38 per cent to 0 per cent. However, he noted that this diet also inhibited estrus and delayed mammary development. With regard to ample exercise and the number of transplanted tumors which developed, Kline and Rusch [4] have not observed difference between rats which had been forced to exercise and the controls.

Diets which are deficient in protein also influence the occurrence and growth of tumors. White and Andervont [5] have shown that there is a lowered incidence of spontaneous mammary tumors in mice on either a

1. Tannenbaum, Albert: Relationship of Body Weight to Cancer Incidence, Arch. Path. **30**: 509 (Aug.) 1940.
2. Potter, V. R.: Science **101**: 105 (Feb. 2) 1945.
3. Morris, H. P.: Science **101**: 457 (May 4) 1945.
4. Kline, B. E., and Rusch, H. P.: Cancer Research **4**: 762 (Dec.) 1944.
5. White, Julius, and Andervont, H. B.: J. Nat. Cancer Inst. **3**: 449 (June) 1943.

lysine or cystine deficient diet. Here again the mammary glands were infantile in development even in mice old enough to be mature. Also there have been studies showing that rats on diets deficient in biotin or pyridoxine show a decreased incidence of tumor formation.

The important question raised by Morris is "To what extent would the dietary regimens found effective in delaying or preventing mouse mammary cancer be effective in delaying or preventing the same disease in man." He concludes that the diets that seem to reduce the incidence of cancer are too drastic, even if they could be applied, to be of any practical value for the prevention of human cancer. Also the effect of exercise was not adequately investigated even in animals, so that definite conclusions cannot be drawn concerning its applicability to human cancer.

Current Comment

VITAMIN C IN HAY FEVER

About three years ago the administration of vitamin C was suggested for the treatment of hay fever and other allergic conditions. Generally this therapy has been viewed with skepticism, but nevertheless some have given it fair trial. Most recent of the reports is that of Friedlaender and Feinberg,[1] who found that hay fever patients have a normal level of vitamin C; although large doses of this vitamin produce saturation blood levels, they do not change the course of hay fever or asthma. In view of this and previously published evidence vitamin C therapy for hay fever and other allergic conditions may be considered useless and wasteful.

RADIOCYSTITIS

Chronic actinic injury following the therapeutic use of roentgen rays and radium is most thoroughly studied and most often noted in the skin, but it occurs not infrequently in internal organs incidentally exposed to radiation. The delayed and insidious development of such reactions, obscuring the causal interrelations, and the inaccessibility of the internal organs to direct inspection are responsible for the smaller degree of attention these lesions have received. Since the urinary bladder is situated within the beam of roentgen and radium rays used for the treatment of neoplastic and other conditions of the uterus, prostate, bladder and rectum, acute and late actinic injuries to this organ are relatively common.[1] Dean [2] noted that all patients receiving more than 3,500 mghrs. of radium therapy, or its equivalent by high voltage roentgen rays, would very likely develop injury of the bladder from the therapy itself, that 27 per cent of all patients treated in this region with actinic rays required prolonged care for vesical distress and that 14.5 per cent had serious lesions of the bladder, such as ulcers and necroses. The therapeutically important actinic injury to the bladder is of the delayed type, appearing six to twelve months after treatment, or the late type, one to nine years after treatment. Such injury is associated with anatomic changes in the vesical wall, namely bullous edema, congestion, telangiectasis, superficial or deep ulcerations, calcareous incrustations and deposits, and causes severe pain, burning sensation on urination, polyuria, tenesmus and hematuria. The functional and anatomic phenomena may resemble closely those in tuberculosis or primary or secondary cancer of the bladder. Biopsy may be necessary at times for differential diagnosis. In the bladder are degenerative and proliferative changes in the epithelium, with swollen and often grotesquely distorted cells, forming not infrequently syncytial masses with large nuclear bodies. There occur ulcerative defects and fibrosis of the submucosa with telangiectasis. Since obliterative endarteritic lesions are not prominent they do not explain the degenerative lesions. Experimental studies on roentgen cystitis in dogs [3] have shown that the injured bladder tends to become infected by fecal bacteria. This infection is refractory to the usual treatment. For this reason patients subjected to actinic therapy involving the bladder should be kept under close urologic supervision so that adequate therapeutic measures may be started on the first signs of radiocystitis, as the control of the fully developed condition is usually protracted and often unsatisfactory.

ANTIBIOTICS

The terms "antibiotics" and "antibiotic effect" were suggested by Waksman and his co-workers in the Department of Microbiology, New Jersey Agricultural Experiment Station, Rutgers University. Waksman, Horning and Spencer [1] isolated sixteen strains of Aspergillus fumigatus and three strains of Aspergillus clavatus from stable manure. These two organisms produced, when grown on synthetic mediums, active substances that differed greatly in their chemical nature and biologic activity. They were designated by the authors as "fumigacin" and "clavacin" respectively. Clavacin was found to be particularly active against gram negative bacteria. The distinguishing characteristic of this substance is that it is both bacteriostatic and bactericidal. Subsequently these substances were crystallized [2] and their chemical nature determined. When gliotoxin, present in fumigacin, is removed, the

1. Friedlaender, Sidney, and Feinberg, S. M.: Vitamin C in Hay Fever: Therapy and Blood Levels, J. Allergy **16**: 140 (May) 1945.

1. Chydenius, J. J.: Irradiation Lesions in Radium Therapy of Cancer of Collum Uteri, Acta radiol. **23**: 1, 1942. Farell, D. M., and Hahn, G. A.: Late Injuries Following Treatment of Carcinoma of Cervix, Urol. & Cutan. Rev. **48**: 165 (April) 1944. Goldblatt, M. E.: Postradiation Effects on Bladder and Ureters Following Use of Deep Roentgen Ray and Radium Therapy for Relief of Pathologic Conditions Affecting Uterus and Its Appendages, ibid. **47**: 632 (Nov.) 1943.

2. Dean, Archie L.: Injury of the Urinary Bladder Following Irradiation of the Uterus, Am. J. Obst. & Gynec. **25**: 667 (May) 1933.

3. Hueper, W. C.; Fisher, C. Virginia; DeCarvahal-Forero, J., and Thompson, M. R.: The Pathology of Experimental Roentgen Cystitis in Dogs, J. Urol. **47**: 156 (Feb.) 1942.

1. Waksman, S. A.; Horning, E. S., and Spencer, E. L.: The Production of Two Antibacterial Substances, Fumigacin and Clavacin, Science **96**: 202 (Aug. 28) 1942.

2. Waksman, S. A.: Purification and Antibacterial Activity of Fumigacin and Clavacin, Science **99**: 220 (March 17) 1944.

purified substance retains its antibacterial activity and only a limited toxicity to animals. At about the same time the English workers Chain, Florey, Jennings and Williams [3] isolated the same substance from a strain of Aspergillus fumigatus and described it as helvolic acid. These investigators believed that helvolic acid was not identical with fumigacin because of certain well defined chemical differences, in particular that of containing nitrogen. The nitrogen content is presumably gliotoxin, mentioned by Waksman. However, Waksman believes that helvolic acid is identical with fumigacin in chemical composition, anti-bacterial action and in vivo activity. He also points out that the isolation of claviforme by Chain and his associates was announced simultaneously with that of clavacin. Waksman stresses that much confusion has arisen in this field from the fact that various micro-organisms are capable of producing the same type of antibiotic substance and that many organisms are capable of producing more than one type of substance. Thus Aspergillus fumigatus has the capacity of forming four different antibacterial compounds—spinulosin, fumigatin, fumigacin and gliotoxin. The three different organisms Aspergillus clavatus, Penicillium claviforme and Penicillium patulum produce the same antibiotic substance. Research has revealed a high degree of cell activity by various antibiotic substances on different bacteria. As pointed out by Schatz and Waksman,[4] Mycobacterium tuberculosis is subject to bacteriostatic action of a variety of antibiotic substances, streptomycin, isolated by them, being promising. This substance is effective also against various related organisms, namely Erysipelothrix and Actinomyces griseus, first described by Schatz and Waksman.

3. Chain, E.; Florey, H. W.; Jennings, M. A., and Williams, T. I.: Helvolic Acid, an Antibiotic Produced by Aspergillus Fumigatus, Mut. Helvola Yuill, Brit. J. Exper. Path. **24**: 108 (June) 1943.

4. Schatz, A.; Bugie, E., and Waksman, S. A.: Streptomycin, a Substance Exhibiting Antibiotic Activity Against Gram Positive and Gram Negative Bacteria, Proc. Soc. Exper. Biol. & Med. **55**: 66 (Jan.) 1944.

PENICILLIN AS A FOOD PRESERVATIVE

In pasteurization of milk and nonpressure canning of fruits and vegetables all vegetative forms of bacteria are usually killed. The residual bacterial contaminants usually consist solely of heat resistant spores. On germination these spores are the main source of toxins and other forms of food spoilage. Since the use of strong chemical antiseptics is not feasible with food products, Curran and Evans [1] of the Division of Dairy Research, U. S. Department of Agriculture, tested the possible efficacy of penicillin as a food preservative (sporicide). Washed bacterial spores, entirely free from vegetative cells, were suspended in sterile water or milk. The suspensions were heated to 95 C. for fifteen minutes to precondition the spores for later germination. Previous tests [2] had shown that many aerobic spores remain latent for a long time without such heating. A measured amount of pencillin was then added to each mixture and the mixture incubated at the optimum temperature for germination. At the end of five to twenty-seven hours' incubation the residual penicillin was inactivated by the addition of penicillinase. The mixtures were then plated. The difference between the number of viable spores thus determined and the original spore count was taken as a measure of sporicidal activity. In a typical test an initial milk count of 256 Bacillus subtilis spores per cubic centimeter was reduced to 1.6 spores per cubic centimeter by the end of five hours and to 0.04 spore per cubic centimeter by the end of twenty-seven hours. Five Oxford units of penicillin per cubic centimeter was used in this test. Similar though less rapid sporicidal action was recorded with the spores of all other aerobic bacteria thus far tested. Effect on anaerobic spores has not yet been reported. The extraordinary effectiveness of pencillin in low concentrations against bacterial spores, together with its nontoxic nature, led Curran to suggest the use of penicillin in numerous nonmedical fields, including that of food preservation. Relatively inexpensive crude penicillin presumably would be satisfactory for such uses.

1. Curran, H. R., and Evans, F. R.: Proc. Soc. Exper. Biol. & Med. **58**: 262 (March) 1945.

2. Curran, H. R., and Evans, F. R.: J. Bact., to be published.

IN VITRO GROWTH OF THE MALARIA PARASITE

The growth of the infective agent in vitro is an important achievement in the investigation of a disease. Whether the emphasis is immunologic, biochemical, nutritional or chemotherapeutic, growth of the parasite in vitro eliminates many secondary or masking effects which the body of the host produces. Recently Ball and his associates [1] have grown the monkey malaria parasite Plasmodium knowlesi in vitro; the medium consists of one-third whole blood and two-thirds purified nutrient solution. Under these conditions it is possible to have the number of organisms increase three or four fold in a twenty-four hour period. With this new method of attack the distribution of phosphorus among the various types of compounds and the oxygen consumption of the organism were determined. Stimulated by the early success, work is in progress on the growth of the human malaria parasite under these conditions. The increasing importance of this disease in the nation's health emphasizes the need for more knowledge regarding the life processes of the infective agent; hence the foregoing experimental device merits further attention.

1. Ball, E. G.; Anfinsen, C.; Geiman, Q. M.; McKee, R. W., and Ormsbee, R. A.: Science **101**: 544 (May 25) 1945.

FOURTH OF JULY FIREWORKS ACCIDENTS

For many years annual summaries of the injuries from fireworks occurring throughout the nation in celebration of the Fourth of July were published in THE JOURNAL. These summaries were influential in bringing about legislation in many states which sharply reduced the frequency of these unnecessary accidents. The fine record of recent years in this respect should be continued. Every effort should be made to curb the use of fireworks on this holiday in order to keep the inevitably attendant injuries at a minimum.

MEDICINE AND THE WAR

ARMY

GERMANY'S TECHNIC IN SURGERY LAGGING

Germany, once the world's acknowledged leader in surgery and medicine, is twenty years behind American methods in the handling and healing of war wounded, according to Col. Edward D. Churchill, Allied Mediterranean forces' surgical consultant, who recently inspected the wounded in former German hospitals. A German army colonel indicated that he regarded the outcome of wounds in this war to be identical with conditions he observed in the first world war. American recoveries, on the other hand, improved phenomenally, such as field operating tents up at divisional clearing stations, the highly developed use of blood transfusions and the high standard of antisepsis in the field.

In the six German hospital areas inspected by Colonel Churchill he found that of forty serious chest wounds picked at random thirty-seven showed infection, while the American patients' average was well below 10 per cent. For blood transfusions the Germans used an antiquated syringe type apparatus discarded years ago by the Americans. The Germans had not realized the possibilities of transfusion and would not believe, until the Americans gave a demonstration, that one man could successfully receive more than 600 cc.

The fundamental difference found between the American and the German system is that the Americans have a systematic, continuous routine from the moment of wounding until the highest possible degree of restoration to health. Infected chest wounds, which after the first world war left hundreds permanently hospitalized with great gaping wounds, can now be handled so that within a few weeks the men are completely restored with normal respiratory systems. The Germans' methods, on the other hand, were characterized by a lack of direction or any general and definite policy in professional methods. Colonel Churchill stated that individual surgeons carried on "just about as they pleased" and field surgeons were inclined to pass over extremely serious cases with the idea that the injured men would die anyway.

LOCAL APPLICATION OF CRYSTALLINE SULFONAMIDES DISCONTINUED

The War Department Technical Bulletin of Medicine (TB MED 147), March 1945 (distributed to general and field hospitals and other medical units), announced the general policies regarding the local use of chemotherapeutic agents. Experience in wound management justifies the abandonment of local use of any chemical agent in a wound for its supposed antiseptic effect in the prevention or treatment of infection. The practice of routine local application of crystalline sulfonamides to wounds as an emergency aid measure and prior to initial wound surgery will be discontinued. The local application of these compounds to wounds not involving serous cavities following wound surgery will also be discontinued, and their local use in wounds involving serous cavities is not recommended.

ARMY AWARDS AND COMMENDATIONS

Colonel Cornelius P. Rhoads

Award of the Legion of Merit was recently bestowed on Col. Cornelius P. Rhoads, formerly of New York. He was cited for the development of methods for combating poison gas and other advances in chemical warfare. Dr. Rhoads was head of the Chemical Warfare Service's Medical Division from June 1943 to April of this year, and he established the Toxicological Research Laboratory at Edgewood Arsenal, Md., and the Medical Research Laboratory at the Dugway Proving Ground, Tooele, Utah. "He developed new methods of diagnosis and treatment for relief of injuries due to toxic chemicals and perfected a compound to counteract the effects of blister gas. At Bushnell, Fla., and San Jose Island, Canal Zone, he established medical testing stations. He also developed equipment for detecting the presence of war gases in air, food and water." Dr. Rhoads graduated from Harvard Medical School, Boston, in 1924 and entered the service June 15, 1943.

Captain Douglas Lindsey

The Silver Star was recently awarded to Capt. Douglas Lindsey, formerly of Minden, La., "for gallantry in action against the enemy in Germany. On . . . during the assault across the . . . River, Capt. Lindsey, battalion surgeon, braved heavy small arms and artillery fire to reach and administer medical treatment to a helpless wounded rifleman. His courageous conduct and professional skill throughout the early stages of this attack were material factors in the prompt treatment of casualties. Capt. Lindsey's exemplary devotion to duty under hazardous conditions reflects great credit on himself and the military service." Dr. Lindsey graduated from Yale University School of Medicine, New Haven, Conn., in 1943 and entered the service Jan. 12, 1944.

Captain Edwin S. Kessler

The Bronze Star was recently awarded to Capt. Edwin S. Kessler, formerly of Cleveland Heights, Ohio, for "heroic achievement in connection with military operations against the enemy during his division's historic reduction of Metz." He directed operations of a battalion aid station in a highly distinguished manner, despite continuous exposure to enemy fire, and his heroic performance of duty was instrumental in saving many lives. Dr. Kessler graduated from Western Reserve University School of Medicine, Cleveland, in 1942 and entered the service July 16, 1943.

Major Sylvan W. Simon

Major Sylvan W. Simon, formerly of Chicago and now with the Air Service Command in Italy, was recently awarded the Bronze Star after he led his medical detachment in stamping out a civilian smallpox epidemic before it reached the thousands of combat airmen of the 15th Air Force who were on duty at nearby airfields. Dr. Simon graduated from Rush Medical College, Chicago, in 1926 and entered the service in October 1940.

Captain John J. Goldsberry

Capt. John J. Goldsberry, formerly of Worcester, Mass., recently received a letter of commendation from the Surgeon General for his origination of the basic idea of a furlough pamphlet as an aid in the prevention of venereal disease in soldiers while on furlough. The commendation read "To the knowledge of this office, Capt. Goldsberry was the first station venereal control officer to organize an effective program aimed at reducing the incidence of venereal disease acquired on furlough and is to be commended for his initiative and originality." Dr. Goldsberry graduated from Howard University College of Medicine, Washington, D. C., in 1926 and entered the service May 12, 1941.

Major James J. Whitsitt

Major James J. Whitsitt, formerly of Houston, Texas, who was with the Airborne troops in the Normandy invasion, was recently awarded the Bronze Star, the Presidential Unit Citation and the Purple Heart, the latter for mortar fire wounds in the leg and thigh. He is now in Germany. Dr. Whitsitt graduated from the University of Tennessee College of Medicine, Memphis, in 1932 and entered the service Aug. 18, 1942.

Major E. Charles Powell Jr.

The Bronze Star and the Meritorious Service Unit Plaque was recently awarded to Major E. Charles Powell Jr., formerly of Goldsboro, N. C. The citation accompanying the Bronze Star read "For meritorious service in connection with military operations against the enemy in Belgium and Germany, November 18, 1944 to March 5, 1945. As regimental surgeon during this period Major Powell, by his display of outstanding administrative ability, technical knowledge and loyalty, supervised the treatment and evacuation of wounded and sick personnel of his regiment under the difficulties of combat conditions and adverse weather in a manner which has insured prompt and efficient medical care. The preventive measures instituted by him during the months of winter warfare were largely responsible for the reduction of frostbite casualties within his unit. The skill, exemplary action and commendable conduct exhibited by Major Powell reflect high credit on himself and the military service."

The citation accompanying the Meritorious Service Unit Plaque read "The Medical Detachment, 334th Infantry, is awarded the Meritorious Service Unit Plaque for superior performance of duty in the accomplishment of exceptionally difficult tasks, Nov. 19, 1944 to March 18, 1945. During this period the members of the unit, maintaining a high standard of discipline and displaying courage despite heavy enemy fire and adverse conditions, administered medical aid and evacuated casualties from the field of battle in a manner which resulted in saving the lives of many soldiers and contributed materially to the success of the regiment's military operations. The brave, unselfish action and commendable conduct of the members of the Medical Detachment, 334th Infantry, reflect high credit on the unit and the armed forces of the United States." Dr. Powell graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1935 and entered the service Sept. 15, 1940.

Major Samuel H. Flowers

The Bronze Star was recently awarded to Major Samuel H. Flowers, formerly of Middlesboro, Ky., "for meritorious service in direct support of combat operations during the period Feb. 10, 1944 to Nov. 20, 1944. Serving Air Force combat units, Major Flowers as surgeon of this hospital (34th Field Hospital) was on call twenty-four hours a day to administer surgical aid to wounded personnel of returning combat crews. Through his devotion to duty and his unstinting efforts beyond the call of duty, Major Flowers has contributed substantially to the combat efficiency of the units served by this organization, and his outstanding service reflects great credit on himself and the Armed Forces of the United States." Dr. Flowers graduated from the University of Louisville School of Medicine in 1931 and entered the service June 20, 1943.

Lieutenant Colonel Noah Barysh

Lieut. Col. Noah Barysh, formerly of New York City, was recently awarded the Bronze Star. The citation accompanying the award read "For meritorious achievement in connection with military operations against the enemy in the North African theater of operations from Nov. 8, 1942 to May 17, 1943. The professional skill, personal courage and untiring energy with which Colonel Barysh performed his duties as regimental surgeon contributed immeasurably to the prompt and efficient treatment of battle casualties throughout the North African campaign. Colonel Barysh's outstanding devotion to duty reflects great credit on the Army of the United States." Dr. Barysh graduated from Rush Medical College, Chicago, in 1933 and entered the service Dec. 21, 1940.

Lieutenant Colonel Julius Sandhaus

Lieut. Col. Julius Sandhaus, formerly of Lancaster, Pa., was recently awarded the Bronze Star for developing what was originally designed as a 40 bed crash ward at an Air Service Command depot in England into a modern, fully equipped hospital, capable of meeting the medical needs of an American city of 35,000 people. Dr. Sandhaus graduated from Jefferson Medical College of Philadelphia in 1936 and entered the service in January 1941.

Captain Harvey L. Rittenhouse

The Bronze Star was recently awarded to Capt. Harvey L. Rittenhouse, formerly of Albany, N. Y. The citation read, in part, "Capt. Harvey L. Rittenhouse, . . . while serving with the Army of the United States, distinguished himself by meritorious service in France. Captain Rittenhouse has been fulfilling his combat mission as medical officer in charge of Ward Section, Second Platoon, from the time the company began operations under combat conditions, Aug. 10, 1944, to the present. During this time he has repeatedly demonstrated his skill and devotion to duty, which has resulted in superior medical service to the patients." Dr. Rittenhouse graduated from the College of Medical Evangelists, Los Angeles, in 1943 and entered the service Aug. 7, 1943.

Colonel Julius M. Blank

The Legion of Merit was recently awarded to Col. Julius M. Blank, formerly of New York City, "for exceptionally meritorious conduct in the performance of outstanding service in New Guinea from Oct. 7, 1942 to April 3, 1943." The citation accompanying the award stated that Colonel Blank "planned, recommended and executed policies for American medical supply, sanitation, hospitalization and evacuation and greatly assisted in the coordination with Allied forces of these matters, which were very important in this area." Dr. Blank graduated from Long Island College of Medicine, Brooklyn, in 1916 and entered the service July 17, 1942.

Major George L. Seifert

The Air Medal with an Oak Leaf Cluster was recently awarded to Major George L. Seifert, formerly of Philadelphia, "for meritorious achievement while participating in sustained operational flight missions to areas where hostile contact was probable and expected." Dr. Seifert graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1934 and entered the service in August 1942.

Captain Robert W. Leibold

Capt. Robert W. Leibold, formerly of Pittsburgh, was recently awarded the Bronze Star for meritorious service in Germany. During a series of operations against the enemy he assisted materially in the treatment, care and evacuation of a large number of wounded men. Dr. Leibold graduated from the University of Pittsburgh School of Medicine in 1941 and entered the service Aug. 1, 1942.

Captain Jesse B. Caldwell Jr.

Capt. Jesse B. Caldwell Jr., formerly of Cramerton, N. C., was recently awarded the Bronze Star "for meritorious service in connection with military operations against an enemy of the United States in France, Belgium, Luxembourg and Germany from Nov. 6, 1944 to March 22, 1945." Dr. Caldwell graduated from McGill University Faculty of Medicine, Montreal, in 1941 and entered the service July 1, 1942.

Major John S. Bralliar

Major John S. Bralliar, formerly of Rockford, Ill., and now commanding officer and chief surgeon of a portable surgical hospital in the Philippines, was recently awarded the Bronze Star "for meritorious service on Luzon." Dr. Bralliar graduated from the University of Tennessee College of Medicine, Memphis, in 1939 and entered the service Dec. 4, 1940.

Captain Paul A. Nierling

Capt. Paul A. Nierling, formerly of Cresco, Iowa, was recently awarded the Bronze Star for meritorious achievement in connection with military operations against the enemy at Luzon. Dr. Nierling graduated from the State University of Iowa College of Medicine, Iowa City, in 1932 and entered the service Nov. 3, 1942.

Captain Lyle B. Putnam

Capt. Lyle B. Putnam, formerly of Wichita, Kan., has been awarded the Silver Star, a Presidential citation and the Purple Heart. Dr. Putnam graduated from the University of Kansas School of Medicine, Kansas City, in 1936 and entered the service in June 1942.

NAVY

NAVY INTERN TRAINING OUTLINED IN NEW BOOKLET

A booklet entitled "Essentials of Internship and Residency-Type Training in United States Naval Hospitals" (Navmed 762) has been prepared by the Professional Division, Bureau of Medicine and Surgery, and is now available for general distribution. This outline was initiated by the Honorary Consultants to the Surgeon General of the Navy. It describes the educational standards and program including uniform hospital libraries necessary to maintain official approval for internship training and for residency-type training in the specialties.

Its foreword by Vice Admiral Ross T. McIntire, Surgeon General of the Navy, states that "junior medical officers assigned to specialty services in naval hospitals will not be termed residents, nor will such services be designated formally as residencies. However, as far as the educational program for such services and assignments conforms with approved residency-type training standards, residency credits will be obtainable by junior medical officers for time engaged in such work while in naval service."

It is possible also for many medical officers assigned to larger dispensaries and other activities to obtain similar residency credits before the American colleges and the American boards.

NEW BRANCHES CREATED IN PROFESSIONAL DIVISION

Vice Admiral Ross T. McIntire, Surgeon General of the Navy, recently approved a reorganization of the Medicine and Surgery Branch of the Professional Division creating two branches of the specialties, namely a Medicine Branch and a Surgery Branch. Capt. F. R. Hook (MC), U.S.N., will head the Surgery Branch, and Comdr. J. R. Miller (MC), U.S.N.R., will head the Medicine Branch. The latter branch is composed of a General Medicine Section and a **Tropical** Medicine Section.

Functions of the Professional Division are defined as follows:

"The Professional Division shall (*a*) consult with medical activities ashore and afloat in order to determine the professional needs and problems arising in the field; (*b*) study, evaluate, advise and make recommendations on the professional needs, policies, standards, practices and performances of the Medical Department, particularly as these relate to medicine, surgery, neuropsychiatry, rehabilitation and hospitalization, and (*c*) maintain liaison with such other military and civilian agencies as may be required in the prosecution of the functions of this division. The term 'professional' as used is interpreted to include all phases of clinical practice as well as the technical services and facilities required to make such practice effective."

HOSPITAL CORPS OFFICER AWARDED LETTER OF COMMENDATION

A Letter of Commendation was recently awarded to Lieut. (jg) William A. Breathwit (HC), U.S.N. The citation, which was signed by Admiral Harold R. Stark, U.S.N., read "Your performance of duty while serving at a large naval base hospital in southern England prior to and after the invasion of the coast of France in June 1944 has been brought to my attention. You were instrumental in the organization and efficient operation of this hospital from its very inception. During the formative period you carried the responsibility for much of the detail work involved in the transfer of the hospital from the U. S. Army. You effectively assisted in the organization of the facilities established for the reception and evacuation of casualties. In addition to your regular duties, which were complex and skilfully carried out, you were invariably present during the admission and evacuation of large groups of casualties, to render what services you could in the interest of efficiency. Your work in the personnel department and in charge of the expeditious and correct reporting of casualties was of high order and contributed materially to the successful work of the hospital. For your devotion to duty and administrative ability you are hereby commended. This commendation carries with it the privilege of wearing the commendation ribbon."

RHEUMATIC FEVER UNIT ESTABLISHED

The Secretary of the Navy has approved a 400 bed expansion of hospital facilities and the establishment of a rheumatic fever research unit at the U. S. Naval Hospital, Dublin, Ga. Commissioned earlier this year, the hospital at Dublin is of permanent type construction, as will be the buildings under the expansion program. However, the building to house the research unit will be a temporary structure. It is slated to begin at once and to be completed about August 30. The hospital at Dublin is used almost exclusively for rheumatic fever cases, and officials in charge of the research project there will work closely with the hospital authorities.

ESTABLISHES ASSISTANT FOR DENTISTRY

Vice Admiral Ross T. McIntire, Surgeon General of the Navy, recently announced the establishment of the post of assistant for dentistry in the Bureau of Medicine and Surgery under whom the functions of the Dentistry Division and the Office of Inspector of Dental Activities will be carried on in accord with a new organizational plan for dental activities in the bureau. Rear Admiral Alexander G. Lyle (DC), U.S.N., has been named the assistant for dentistry and has served for some months in the bureau as inspector of dental activities.

The functions of the assistant for dentistry were defined as follows: The assistant for dentistry shall be responsible for the performance of all dental functions but shall adopt no major policies, methods or procedures without the approval of the chief of the Bureau of Medicine and Surgery. The assistant for dentistry may have on his personal staff such other personnel as may be required to assist him in the general administration of his duties.

The organizational plan announced included, besides establishment of the assistant for dentistry, a Dental Professional Office, a Dental Personnel Office and a Dental Inspections Office.

WAVE HOSPITAL CORPS TRAINING SCHOOL

Camp Moffett, one of the larger units of the Naval Training Center at Great Lakes, Ill., is being converted for use as a Hospital Corps School to accommodate 1,500 Waves under plans approved by the Bureau of Medicine and Surgery. It is expected that conversion will be completed in time to take the first increment of recruits from Hunter College the latter part of July.

Beginning with the first class, the Hospital Corps will receive 500 girls each two weeks for training. One hundred and twenty-five of these will be given eight weeks' training at Bethesda and 375 will be sent to the new unit at Great Lakes for their schooling. At the end of an eight week period both schools will have reached their full capacity: 500 at Bethesda and 1,500 at Great Lakes. This schedule is slated to continue through a period of ten months, at the end of which time the Hospital Corps will have trained 10,000 additional Waves.

NAVY AWARDS AND COMMENDATIONS

Commander DeWitt K. Burnham

The Legion of Merit was recently awarded to Comdr. DeWitt K. Burnham, formerly of San Francisco. He was cited for "exceptional performance of duty, clearly above that normally expected" while on duty in the South Pacific. Through his "untiring efforts in maintaining sanitary standards, he has reduced the incidence of sickness and disease to a remarkably low degree and provided necessary medical attention for all personnel at the base," the citation said, adding that Commander Burnham had instituted a "highly efficient system for handling large numbers of patients and casualties from hospital ships." Dr. Burnham graduated from Stanford University School of Medicine, San Francisco, in 1930 and entered the service Dec. 18, 1941.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

June 18, 1945.

Possible Release of Doctors and Dentists from Armed Forces

Major Gen. George F. Lull, Deputy Army Surgeon General, has estimated here that 2,000 to 3,000 doctors and several hundred to 1,000 dentists should be available for discharge from the Army by the end of this year. General Lull said the peak load on the Army Medical Corps will be reached in the fall. He explained that the wounded must still be transported home from Europe and soldiers scheduled for redeployment or discharge must be given physical examinations. He expects that most of the doctors and dentists released will return to civilian practice. The Veterans Administration has sought medical men, but its most urgent requirements were met by assignment of about 300 medical officers to the agency, he said. Most of these were assigned last year on active status, and 112 had previously served with the Veterans Administration. However, no Army doctors are now being assigned to the Veterans Administration unless they desire it. General Lull said that "as the size of the Army is reduced under the partial demobilization plan, it will be possible to release certain numbers of doctors and dentists. However, the shrinkage in the number of medical officers will not be in proportion to the reduction of the Army as a whole, since the Army will still have many wounded in hospitals. Moreover, we never filled our quota of 48,000 doctors, as only about 45,000 were obtained. Dental officers number about 15,000. We probably can release 2,000 to 3,000 medical officers and a proportionate number of dental officers by the end of the year."

General Bradley to Take Veterans Administration Post August 11

Although he conferred with members of the House Veterans Committee on proposed veterans' legislation and has already started a study on how to correct shortcomings in the administration of veterans' hospitals, General Bradley has returned to Europe to serve in the absence of General Eisenhower. He will take over as Veterans Administration chief about August 11. Meanwhile Committee Chairman Rankin has reported that hearings on proposed legislation to reorganize the medical staff of the Veterans Administration will be postponed until General Bradley returns. "We will continue with the investigation to have a full record for General Bradley and the committee," he said. "It will serve as a basis for corrective legislation." Before adjournment the committee heard Col. Louis Verdel, manager of the veterans' hospital at Northport, N. Y., where it was alleged that the Army had assigned physically and mentally unfit soldiers to attend mental patients, deny that Northport was the worst hospital in the service. He claimed that two of five army doctors attached to the institution were on prolonged sick leave, one of them diagnosed as neurotic by army examiners. "Maybe we'd better investigate the War Department," said Mr. Rankin. "I bitterly resent the War Department's attitude toward these veterans' hospitals."

Naval Medical Chief Lauds Care of Wounded on Okinawa

Vice Admiral Ross T. McIntire informed civilian and service personnel of the Navy Bureau of Medicine and Surgery that navy medical men caring for troops wounded on Okinawa "have lacked nothing" in supplies and equipment. His comment was made during presentation of awards to personnel for beneficial suggestions and achievement.

Capital Notes

Sister Elizabeth Kenny told a press conference that the purpose of her two months trip to England and Sweden was to "stimulate research" in infantile paralysis in these two countries rather than to set up clinics.

Gallinger Hospital plans to take an active part in the postgraduate education of doctors returning from the armed forces, Dr. Daniel L. Seckinger, acting superintendent, announces.

District of Columbia's new mental hygiene clinic has reached a stalemate through the sudden resignation of Dr. John F. Owen of Raleigh, N. C., after only a month, because of inadequate office and clinic space provided.

Council on Medical Service and Public Relations

PREPAID MEDICAL CARE NEWS

Washington Medical and Hospital Service Plan

In reviewing the history of medical bureaus in Washington, it has been noted that in 1931 and 1932 several service bureaus were started in counties throughout the state where population would warrant. As there was a close relationship of one county bureau to another and a reciprocal agreement between their physician members, the Washington State Medical Bureau was set up as a coordinating and parent body. While the local county bureaus, of which there are now seventeen, exercise certain local autonomy to meet the needs of their respective communities, the plan as a whole is statewide and is referred to as the "Washington Plans." It is under the supervision and guidance of the Washington State Medical Association and is administered by the Washington State Medical Bureau.

Medical service bureaus have carried out the service policy, and in order that they may be legal in every respect to meet requirements of the insurance code the physician members of the bureaus personally organized and financed an insurance company, which places the Washington State Medical Bureau and its component county bureaus under the supervision of the state insurance department, which in turn certifies as to the financial stability through adequate reserves deposited with it. The sole purpose of the insurance company is to legalize and guarantee the fulfilment of the medical service contracts issued by the bureaus.

Many unions, realizing the benefits to their members, have contracts covering their membership. The relationship between the unions and the medical service bureaus is one of real cooperation to the mutual benefit of the bureaus and the recipients of the service. The assistance rendered by the committees of the unions has been of great value in determining policy and coverage.

Last year the bureaus provided hospital coverage for the family, but it was realized that this was only partially solving the problem. The family of the wage earner should also be provided with professional care if he is to have medical economic security.

With the approval and endorsement of their many thousands of subscribers, the bureaus are now writing a family coverage that not only provides hospitalization for all medical and surgical cases but also pays for the doctor's services in all accident cases, major and minor operations, fractures, dislocations and other surgical procedures. This leaves the subscriber to pay only for the occasional office or house calls, which do not constitute an economic problem. The wage earner really has medical economic security, and the doctors of the state of Washington have found a way to provide it on a voluntary basis free from government intervention or at the expense of the taxpayer.

In 1935, when the need of providing medical care to recipients under the general assistance program was recognized, the state department of social security appointed the medical service bureaus as administrators of the medical and dental program in their respective counties. In 1941, when legislation was enacted providing complete, adequate medical care to recipients of old

age assistance, the medical service bureaus were again appointed administrators for that program.

The doctors through their medical service bureau have demonstrated their ability to manage all programs pertaining to medical care and its allied service. What they have done in Washington can likewise be done elsewhere. So say the progressive physicians of Washington.

Liberalization of Michigan Medical Service

Increase of benefits to subscribers with no increase in rates has been announced by Michigan Medical Service. The additional benefits were made effective April 1 and were enabled by the unusually strong financial position of the Michigan plan. Nearly 800,000 subscribers are entitled to the new benefits.

Among the liberalizations are removal of the previous limit of $150 for surgical service provided under the schedule of benefits and performed at the same time or for the same purpose, elimination of the waiting period on other obstetric services and provision for emergency surgical services for doctors in hospital outpatient departments.

Michigan Medical Service is sponsored by the Michigan State Medical Society. Its companion organization, Michigan Hospital Service, also instituted an increase in benefits on April 1, but an increase in subscriber rates was necessary to provide for the hospital service increase.

Ohio Medical Indemnity, Inc., Organized

Additional steps toward the organization of a medical, surgical and obstetric expense insurance company were taken by the officials of the Ohio State Medical Association on May 23, when articles for the incorporation of a company, to be known as "Ohio Medical Indemnity, Inc.," were filed with the secretary of state.

Negotiations with the superintendent of insurance for approval of its policy, schedule of benefits and rates, preliminary to the issuance by the superintendent of a certificate of authority to operate in Ohio, will be opened as soon as the company receives its charter from the secretary of state.

According to Dr. L. H. Schriver, Cincinnati, president of the Ohio State Medical Association and one of the incorporators, the new company plans to work closely with the prepaid hospital service—the Blue Cross—organizations of Ohio, making use of the sales, promotion, clerical and certain administrative facilities of the Blue Cross plans.

Two Savings Banks Subscribe to United Medical Service

Two more savings banks have subscribed to the expanded plan of United Medical Service, Inc., for the payment of doctors' bills in addition to surgeons' and obstetricians' bills in hospitals, it was announced on May 31 by Frank Van Dyk, vice president. They are the New York Savings Bank, with 120 employees, and the South Brooklyn Savings Bank, with a personnel of 132. Both banks are paying the cost of this service and of hospitalization under the Associated Hospital Service of New York for employees and their families.

Illinois Insurance Committee Makes Study

Dr. Charles H. Phifer, chairman of the Illinois committee, reports that "this committee has been currently engaged in making a special study of all prepayment plans for medical, surgical and hospital care in the United States. The committee has interviewed representatives of industrial organizations, railroads, insurance carriers, agricultural organizations, charitable hospitals and institutions in the state of Illinois. It likewise interviewed the medical representatives of the neighboring states regarding prepayment plans for medical, surgical and hospital care that are operating in their states or are in the process of formation."

Indiana Subdivides Committee Duties

Dr. W. U. Kennedy of New Castle, chairman of the Committee on Prepayment of Medical and Surgical Care, has divided his committee into three subcommittees each studying separate phases of the insurance problem. These subcommittees are ready to make their reports to the parent committee, which in turn will report to the House of Delegates.

New York Group Health Plan Adds Visiting Nurse Service

Group Health Cooperative, 70 Wall Street, announced on June 1 that, through the cooperation of the Visiting Nurse Service of New York, the Visiting Nurse Association of Brooklyn and the Visiting Nurses Association of Staten Island, it will provide visiting nurse service for subscribers to its medical care insurance plan at no increase in premiums. This is the first time that visiting nurse service has been included in a voluntary health insurance plan.

Subscribers will be entitled to the amount of service their doctors consider necessary in any illness covered by the medical plan. The group health plan provides insurance against doctors' services for any surgical care rendered in the home or doctor's office. The plan also covers maternity care.

The visiting nursing agencies in New York City have welcomed the opportunity offered by Group Health Cooperative to demonstrate the value of nursing services in connection with voluntary prepaid medical plans.

Missouri Medical Service Plan Launched

Missouri Medical Service, the nonprofit medical service plan through which Missourians may voluntarily enroll to obtain medical and surgical care in hospitals, was launched Monday, March 12, according to Dr. Carl F. Vohs, St. Louis, president of the new medical plan and chairman of the Medical Economics Committee of the Missouri State Medical Association. The plan is sponsored by the state medical association and local county medical societies throughout Missouri, comprising 3,250 doctors.

Enrolment in the plan will be offered through Blue Cross of St. Louis. The two organizations are separate, but considerable economy will be effected through management of the medical and surgical care plan by the Blue Cross.

At the outset, enrolment in the plan will be open only to the 480,000 employees of firms in Missouri which are members of the Blue Cross. Those belonging to Blue Cross will now have available a complete program for care while in hospitals.

Dallas Service Plan Expands

The recent appointment of Mr. Millard J. Heath as full time executive director of the Dallas County Medical Plan marks the first step in a program of expansion. For about five years this prepaid plan, which is sponsored by the Dallas County Medical Society as a nonprofit medical care plan for low income groups, has been operating on a limited basis with three industrial groups. It is now believed that the time has come to make the service available to a much larger group, and a survey is being made of major industries to determine their interest and possibility of participation. Enrolment is being offered only to employed persons, but the extended services include a consideration of wives and other dependents as soon as practicable. Subscribers are being offered complete medical care in the home, office or hospital, including surgery, x-ray and laboratory work.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Medical and Dental Corps

Senator Downey, California, has submitted S. Res. 134, proposing that the Senate Committee on Military Affairs or a subcommittee thereof be directed to make a complete investigation as to the relative needs of the armed forces and the civilian population for the services of medical personnel with a view to ascertaining (1) whether such personnel can be released from the armed forces for civilian service without impairment of the war effort, (2) the speed with which demobilization of medical personnel in the armed forces can be accomplished as the needs of the armed forces diminish and (3) whether further action is necessary to insure an adequate supply of trained medical personnel to meet the future needs of the armed forces and the civilian population.

A bill to remove the limitation on the right to command of officers of the Dental Corps of the Army which limits such

officers to command in that corps, S. 916, has passed the Senate and has been favorably reported by the House Committee on Military Affairs.

A bill has been favorably reported to the House, H. R. 2477, proposing that during the present war and for six months thereafter an enlisted man of the Army who is entitled to wear the Medical Badge shall be paid additional compensation at the rate of $10 a month.

Dental Health

The Pepper Subcommittee on Wartime Health and Education has scheduled hearings for June 26, 27 and 28 on S. 190, proposing the establishment of a National Institute of Dental Research, and on S. 1099, proposing assistance to states in developing and maintaining dental health programs.

Veterans Administration

A bill has been introduced in the House by Representative Voorhis, California, H. R. 3463, proposing the creation of a National Veterans' Hospital Board with the following duties: (*a*) to advise the Administrator of Veterans' Affairs on all matters pertaining to the hospital or outpatient care of veterans and concerning the appointment of a National Executive Director for all veterans' hospitals; (*b*) to conduct a complete survey of all veterans' hospitals and to recommend to the Administrator and the National Executive Director such changes in personnel, such hospital construction and such other action as may be necessary; (*c*) to consult with the Administrator and the Director on the appointment of chief medical officers for all veterans' hospital units in the United States; (*d*) to provide adequate arrangements and facilities for continuous research on improved methods in the fields of medicine, psychiatry and all other types of care required by veterans; and (*e*) to prepare a schedule of proposed salaries, grades and classifications for all types of employees, professional or otherwise, in veterans' hospitals with a view to obtaining competent and qualified personnel.

A bill introduced by Representative Holifield, California, H. R. 3253, proposes to facilitate the receipt of hospital treatment and domiciliary care by former members of the armed forces at institutions nearest to their places of residence.

Three recent bills provide for the construction of new veterans' hospitals. One, H. R. 3428, introduced by Representative Latham, New York, contemplates the construction of such a hospital in the borough of Queens, city of New York, and the other two, H. R. 3475 and H. R. 3476, both introduced, by request, by Representative Rankin, Mississippi, provide for the construction of veterans' hospitals in central and southeastern Alaska, respectively.

Scientific Research

A bill introduced by Representative May, Kentucky, H. R. 3440, proposes an appropriation not to exceed $8,000,000 for each fiscal year to enable the National Academy of Sciences, through a research board for national security consisting of representatives of the Army, of the Navy and civilians of outstanding accomplishments, to provide for scientific research and advancement determined by the board to be desirable in the interest of national security.

Food, Drug and Cosmetic Act

The bill providing for the certification of batches of drugs composed wholly or partly of any kind of penicillin or any derivative thereof, H. R. 3266, has been reported to the House by the Committee on Interstate and Foreign Commerce with the recommendation that it pass. The committee report on this bill, H. Report No. 702, contains a letter from the Council on Pharmacy and Chemistry of the Association in support of the bill.

Miscellaneous

Senator Thomas, Oklahoma, has introduced S. 1123, proposing an appropriation of $1,000,000,000 per year for each of three fiscal years to enable the Federal Works Administrator to make loans and grants to public agencies for the construction of public works projects, including schools, hospitals, nurses' homes, sewerage systems and garbage and refuse disposal facilities.

STATE LEGISLATION

Alabama

Bill Introduced.—H. 448 proposes to enact a separate practice act for vocational nurses and to create a board of six, to be composed ultimately of three physicians and three vocational nurses, to examine and register applicants desiring to designate themselves as vocational nurses.

California

Bill Introduced.—A. 2211 proposes to prohibit a hospital having available facilities from refusing to render emergency medical care to any person who has been injured in an accident and is in need of immediate care. If the individual receiving such services is indigent and unable to pay therefor, the reasonable costs of the services are to be paid by the county.

Connecticut

Bills Passed.—The following bills have passed the house and senate: S. 865 proposing that nothing in the medical practice act shall prevent any student in or graduate from any school or institution giving instruction in the healing arts, approved as provided in the act, from taking supplementary training with any regularly licensed and reputable practitioner or from serving as an intern in a hospital. The present law provides such an exemption for any student in or graduate from any legal and reputable professional school; and Sub. for S. 879 proposing that any resident who has served in the armed forces of the United States and whose moral and educational qualifications are approved by the board of chiropractic examiners shall be licensed to practice chiropractic without examination; and Sub. for H. 1031 proposing to direct the legislative council to make a comprehensive inquiry into the methods of professional and vocational licensing in the state. H. 402 has passed the house, to amend what in effect is the basic science act, proposing to change some detail in connection with the appointment of members of the state board of healing arts. It is proposed that the governor appoint one member of that board before July 1 to serve for six years and that on May 1, 1947 and biennially thereafter the governor shall appoint, *with the advice and consent of the general assembly*, one member to serve for six years. It is proposed also to provide compensation of ten dollars a day for each day of service for members of the board.

Bill Introduced.—Sub. for S. 84, to amend the charter of the Connecticut State Medical Society, proposes that its house of delegates be composed of (1) its president, president-elect, treasurer and secretary, (2) delegates elected annually by the several county medical associations and (3) the members of its council.

Florida

Bill Enacted.—H. 883 became a law without the approval of the governor on June 11, authorizing the creation and operation of corporations to operate nonprofit medical and/or surgical and/or hospital service plans.

Bills Introduced.—S. 704 proposes to authorize the governing board of any governmental hospital to prescribe the qualifications and standards of the physicians who may use its facilities, which qualifications shall require at least two years of service as a hospital intern as a prerequisite to the right to perform surgery. S. 806 proposes to prohibit, except on the prescription of a licensed physician, the retail sale of any sulfonamide drug, penicillin drug or any preparation for the treatment, alleviation or cure of gonorrhea, syphilis or chancroid.

Illinois

Bills Introduced.—H. 719 proposes to enact a practice act for professional chemistry and to authorize the department of registration to appoint an examining committee of nine professional chemists. A person practices professional chemistry within the meaning of the bill "who applies the principles and data of chemistry in any of its branches or phases in determining, governing or regulating the welfare of individual or of industry, or in the exposition of such principles in any oral or written report or in any procedure." H. 749 proposes to enact a bill to regulate the practice of professional bacteriology and to authorize the department of registration to appoint a committee of nine professional bacteriologists to examine appli-

cants for licenses to practice that profession. A person practices professional bacteriology within the meaning of the bill "who makes laboratory examinations in connection with the diagnosis of bacterial or viral diseases of man or animals, who prepares vaccines and antisera, who tests water, milk and other foods for evidence of contamination or the presence of disease producing micro-organisms, who tests surgical sutures and bandages, vaccines, antisera and pharmaceutical drugs for contamination with micro-organisms, who tests antiseptics, disinfectants and other drugs for their killing properties of micro-organisms, who prepares or tests cultures of nitrogen fixing bacteria, who prepares or tests antibiotics, who prepares organic substances by the action of micro-organisms and who assays vitamins, amino acids or other substances by microbiological methods."

Massachusetts

Bills Introduced.—H. 2029 proposes to prohibit the operation of a hospital, sanatorium or convalescent or nursing home without a license from the department of public health. H. 1980 proposes to make Middlesex University School of Medicine an approved medical school until July 1, 1949 and, in effect, to permit its graduates to be examined for licenses to practice medicine.

Ohio

Bill Introduced.—Sub. for H. 62 proposes that the practice of Christian science by a member in good standing of the Christian Science Church shall be lawful.

Official Notes

DOCTORS LOOK AHEAD

Remaining programs in the series of network broadcasts by the NBC and the American Medical Association will be on the air June 23 and 30 except in Chicago.

Doctors Look Ahead is broadcast each Saturday at 4:30 p. m. Eastern War Time (3:30 p. m. Central War Time, 2:30 p. m. Mountain War Time and 1:30 p. m. Pacific War Time) except in Chicago, where each week's program as broadcast on the network will be heard on the next Saturday afternoon at 3 p. m. Central War Time.

June 30. Health in Schools: A program devoted to health education and related topics in our schools, where doctors look ahead to greater progress in the next decade. Speaker Dr. Charles C. Wilson, Teachers College, Columbia University, speaking from New York.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

At its meeting on Sunday, June 10, the Council on Medical Education and Hospitals of the American Medical Association voted to place on probation the Hahnemann Medical College of Philadelphia. This action was based on a detailed survey of the school carried out by the Secretary of the Council and the Secretary of the Association of American Medical Colleges April 3-6, 1945.

A medical school is placed on probation when significant but correctable deficiencies are judged to exist in the educational program. Such an institution remains on the list of approved schools maintained by the Council, with its probationary status indicated by a footnote. Hospitals approved by the Council may appoint graduates of such a school as interns, residents or fellows, and all otherwise qualified students entering or attending a school on probation are considered acceptable to the Council. In fact, so far as the students in residence are concerned, even if a school should be removed from the list of approved schools such action by the Council would become effective only after all students in the school at the time of the announcement of the action have had time to graduate.

The Council will give every assistance to this school in its efforts to improve the educational program sufficiently to warrant removal of the probation.

VICTOR JOHNSON, M.D., Secretary.

Bureau of Information

SUMMARY SHEETS FROM MINNESOTA AND WEST VIRGINIA

Completed county summary sheets have been received from the Minnesota State Medical Association through Mr. R. R. Rosell, executive secretary, and from the West Virginia State Medical Association through Mr. Charles Lively, executive secretary.

The accompanying table gives data from counties in each of these states. The column giving the number of persons per telephone is used as one index of the economic status of the area. Many physicians over 65 years of age are carrying on large practices and are doing much to maintain the health of communities. They are not included in computing physician population ratio, however, as the future needs of the communities will be largely dependent on younger physicians.

A current knowledge of needs of communities for doctors is essential if adequate help is to be given veteran medical officers in their problems of medical practice. These needs can be indicated on the summary sheets under "Remarks" by the state and county secretaries and are then available to inquiring medical officers. Frequent reports from state and county medical societies about needs of communities for doctors will help maintain current files and will increase the service of the Bureau.

With the information available on a completely filled out summary sheet, it is readily possible for an interested medical officer to make an initial selection of areas in which he might like to practice. Since vacancies are held open in many communities for doctors now in military service, further investigation by direct correspondence with state and county medical societies will always be necessary to insure an accurate report of the needs of individual communities.

Minnesota

County [1]	Principal Cities [2]	Population	Physicians Under 65	Persons per Physician	Persons per Telephone [3]
Aitkin		12,856	3	4,285	8
Anoka		23,771			
	Anoka	6,426	6	3,962	17
	Columbia Heights	6,035			
Clay		22,733	9	2,526	9
	Moorhead	9,491			
Dodge		11,173	4	2,793	8
Hubbard		8,783	2	4,392	10
	Park Rapids	2,643			
Lac-qui Park		13,472	5	2,694	9
Lake of the Woods		3,994	1	3,994	10
Mille Lacs		13,212	4	3,303	6
Roseau		12,820	4	3,205	9
Yellow Medicine		15,302	9	1,700	8

West Virginia

County [1]	Principal Cities [2]	Population	Physicians Under 65	Persons per Physician	Persons per Telephone [3]
Barbour		16,457	8	2,057	41
Calhoun		8,839	1	8,839	10
Fayette		71,635	27	2,653	32
	Oak Hill	3,213			
	Montgomery	3,231			
Grant		7,424	3	2,475	81
Jackson		13,948	3	4,649	9
Lincoln		18,487	4	4,622	212
Mason		20,630	5	4,126	28
	Point Pleasant	3,538			
Mineral		19,779	9	2,198	17
	Keyser	6,177			
	Piedmont	2,677			
Wirt		4,935	1	4,935	17
Wyoming		29,700	9	3,300	92
	Mullens	3,026			

1. Bureau of Census, estimated population 1943.
2. Bureau of Census, population 1940.
3. Based on 1940 figures, American Telephone & Telegraph Company.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Compulsory Hospitalization Bill Killed.—The compulsory hospitalization bill, assembly bill 2201, actively supported by Governor Warren, the C. I. O., the A. F. of L., the Parent-Teachers Association and the League of Women Voters, was killed in the assembly June 5. By a vote of 45 to 32 the assembly refused to override the recommendation of its public health committee and withdraw the bill from that committee. The opposition to the bill was presented by Howard Burrell, chief counsel for the Association of California Hospitals, who declared that the measure would "sovietize" the hospitals of California. Dr. Chester L. Cooley, San Francisco, presented the opposition of the California Medical Association and pointed out that the bill was similar to the original compulsory health insurance bills which had been killed by the assembly. Opposition of business groups was presented by Charles Bayer of the Los Angeles Chamber of Commerce and Pat Merrick of the California State Chamber of Commerce.

Activities of Hastings Foundation.—The Charles Cook Hastings Home for the study and treatment of tuberculosis, located north of Pasadena, is expected to open about August 1. Dr. Edward Kupka is medical director of the Hastings Foundation for Tuberculosis Research, Pasadena, set up by the will of Charles H. Hastings, and of the Charles Cook Hastings Home (THE JOURNAL, Dec. 30, 1944, p. 1158). *Science* reports that agreement has been made with the Veterans Administration Facility, San Fernando, to treat 20 veterans of the war who have developed tuberculosis, the entire cost of care to be paid by the Hastings Foundation. Dr. Horace R. Getz, research associate of the Henry Phipps Institute, Philadelphia, is director of the laboratories and will continue research on nutrition heretofore carried on by him in Philadelphia, which will include an attempt to learn the effect of nutrition on the course of tuberculosis. *Science* further reports that objective nutrition tests on the blood and biomicroscopy of the eyes, tongue and gums will be a part of the routine examination of the subjects, all of whom will receive a good standard sanatorium diet with one half being given food supplements. Progress of the disease in the two groups will then be carefully compared.

DISTRICT OF COLUMBIA

Dr. Owen Returns to North Carolina.—Dr. John F. Owen, who on May 1 became director of the new bureau of mental hygiene in the health department of the District of Columbia, has resigned to return to his position as superintendent of the State Hospital, Raleigh, N. C., according to the Washington *Times-Herald,* June 5. Dr. Owen's appointment to the new position was reported in THE JOURNAL, May 19, page 216.

Surveyor Board Named for Hospital Study.—A board of surveyors consisting of Charles E. A. Winslow, Dr.P.H., Col. Ira V. Hiscock, S.C., New Haven, and Dr. Claude W. Munger, New York, was recently named and charged to direct the health and hospital survey sponsored by the Washington Metropolitan Health Council, a division of the Council of Social Agencies, for the Washington Metropolitan area. The survey is expected to be completed within four months starting September 1 and will involve a study of facilities and activities of health agencies, hospitals and clinics, both public and private, in the metropolitan area lying in the District of Columbia, Prince Georges County, Montgomery County, Arlington County, Fairfax County and Alexandria City. The survey has the endorsement of the Community War Fund, the Washington Board of Trade, the Medical Society of the District of Columbia the six health officers of the area and the state commissioners of health of Maryland and Virginia. The Washington Metropolitan Health Council was recently created under the sponsorship of the Council of Social Agencies (THE JOURNAL, January 20, p. 173). Vice Admiral Ross T. McIntire, Surgeon General of the Navy, is chairman of the survey committee and Dr. Herbert P. Ramsey is head of the health division of the Council of Social Agencies.

ILLINOIS

Personal.—Dr. Charles E. Riseling was given a dinner May 2 in honor of his fifty-two years' service to Murphysboro and of forty-eight years' service as a member of the staff of St. Andrew's Hospital, of which he became one of the original members when it was founded in 1897.——Dr. George W. Ross was installed as mayor of Watseka on May 14.

Chicago

Medical Group Practice Council Holds Meeting.—A meeting of the Western section of the Medical Group Practice Council was held at the Palmer House, Chicago, June 6-7, with Dr. Samuel Bradbury, Philadelphia, as chairman. At the luncheon meeting on June 7 Dr. Kingsley Roberts of the Medical Administration Service, New York, presided. Drs. Morris Fishbein and Victor Johnson of the American Medical Association were guests, and Clarence Rufus Rorem, Ph.D., director of the Hospital Plan Commission of the American Hospital Association, also attended. This council is organized under the auspices of the Medical Administration Service, Inc., to promote the extension and improvement of medical group practice by preparing and disseminating publications regarding the standards, procedures, problems and values of this method of distributing medical care.

MARYLAND

Council on Medical Care Created.—A council on medical care has been created by authority vested in the state board of health by act of the 1945 session of the general assembly to provide consultation and advice in connection with the program to be administered by the newly established bureau of medical services (THE JOURNAL, May 12, p. 143). The following have been chosen members of the council to represent the organizations indicated:

Dr. Page C. Jett, Medical and Chirurgical Faculty of Maryland.
Dr. Earle Paul Knotts, Medical and Chirurgical Faculty of Maryland.
Dr. Jacob W. Bird, state board of health.
A. G. DuMez, Maryland Pharmaceutical Association.
Dr. James Douglass Shepperd, Maryland Medical Association.
F. Noel Smith, Maryland State Dental Association.
P. J. McMillin, Maryland District of Columbia Hospital Association.
Dorothy F. McBride, Maryland State Nurses Association.
Dr. Alan M. Chesney, Johns Hopkins University School of Medicine.
Dr. George Carroll Lockard, University of Maryland School of Medicine and College of Physicians and Surgeons.
Dr. Robert H. Riley, director of the state department of health.
Dr. George H. Preston, state commissioner of mental hygiene.
Dr. Victor F. Cullen, superintendent of Maryland state tuberculosis sanatoriums.
J. Milton Patterson, director of the state department of welfare.

Dr. Dean W. Roberts, chief of the bureau of child hygiene of the state department of health, was appointed chief of the bureau of medical services, which will administer a program furnishing medical care for indigent and medically indigent persons and will conduct and operate the chronic disease hospitals to be constructed in the postwar period.

MINNESOTA

Changes in Health Officers.—Dr. Rolv S. Hegge, Austin, has been named health officer of Mower County to succeed Dr. James J. Morrow, Austin.——Dr. Roland F. Mueller, Two Harbors, has been appointed health officer of Lake County.

Health and Medicine in War and Peace.—On June 5 Vice Admiral Ross T. McIntire, Surgeon General of the U. S. Navy, and James L. Morrill, LL.D., president-elect of the University of Minnesota, discussed "Health and Medicine in War and Peace" at a dinner meeting held under the sponsorship of the committee of founders of the Mayo Memorial.

The Johnston Lecture on Neurology.—Dr. Olof Larsell, professor of anatomy, University of Oregon Medical School, Portland, gave the first J. B. Johnston Lecture on neurology, May 11, at the University of Minnesota Medical School, Minneapolis. His subject was "Comparative Neurology and Our Present Knowledge of the Cerebellum." The lecture was endowed by Mrs. Johnston in memory of her husband, John B. Johnston, Ph.D., who served as professor of comparative neurology in the medical school from 1908 to 1915 and dean of the College of Science, Literature and the Arts from 1914 to 1937 (THE JOURNAL, February 3, p. 287).

NEW HAMPSHIRE

State Medical Election.—Dr. Richard W. Robinson, Laconia, was named president of the New Hampshire Medical Society at its annual meeting in Manchester, May 15. Other officers include Drs. Ralph W. Tuttle, Wolfeboro, vice president and Carleton R. Metcalf, Concord, secretary-treasurer.

NEW JERSEY

Ill Award Goes to Dr. Sprague.—The Edward J. Ill Award of the Academy of Medicine of Northern New Jersey was presented to Dr. Edward Wharton Sprague, Newark, during the annual meeting of the academy, May 17, "in recognition of his attainments as a surgeon and his contribution to the public welfare through his service in many civic and social welfare organizations." Dr. Harrison S. Martland, Newark, professor of forensic medicine, New York University College of Medicine, gave the principal address, on "Oh Why Should the Spirit of Mortal Be Proud?"

NEW YORK

Prevalence of Spotted Fever.—In 1944 17 cases of Rocky Mountain spotted fever, 4 of which terminated fatally, were reported in the state, exclusive of New York City, more than in any previous year on record. Although the disease was first recognized in this state in 1912, it has been only in the past decade and particularly in the last six years that a noticeable increase in incidence has been observed. This fact, coupled with the occurrence of sixteen deaths among the total of 86 cases reported from the area, plus what appears to be a gradual extension of the infection from the initial focus discovered in 1912, gives the health authorities in the state some cause for concern, according to *Health News*. Except for a single infection acquired accidentally in a Rockland County laboratory experimenting with the disease, all the cases on record in the New York State Department of Health have been confined to the Long Island area. Since the first 3 cases on record in the state were reported in Gardiner's Island, 2 with onset in 1912 and 1 in 1913, no cases were recognized until 1924, when 1 case was reported at the eastern end of Long Island proper in Suffolk County. Subsequent cases were confined to this county until 1939, when the first infections contracted in Nassau County were reported. In the group of 17 cases in 1944 the ages ranged from 3 to 72 years, about equally divided as to sex. Onsets of illness were confined to the period May through September, 6 in May, 3 in June, 3 in July, 4 in August and 1 in September. In 7 there was a definite history of tick bite and in 6 others evidence of contact with a tick. It is significant that in 8 cases the disease apparently was acquired through contact with tick-infested domestic animals: dogs in 7 cases and a cat in 1 case.

New York City

Marvin Thompson Resigns at Warner Institute.—Marvin R. Thompson, Ph.D., has resigned as president and director of the Warner Institute of Therapeutic Research, effective July 1.

Kellogg Grant to Train Hospital Executives.—The W. K. Kellogg Foundation, Battle Creek, Mich., has given Columbia University a grant of $60,000 to establish a course of training for hospital administrators, the New York *Times* reported June 5. The work will be carried out in the DeLamar Institute of Public Health and will be available for graduate students. The *Times* stated that plans already had been made for the Columbia faculty of medicine to carry out the training program in cooperation with hospitals and other organizations throughout the country.

OHIO

Industrial Commission Adopts Revised Medical and Surgical Fee Schedule.—The Ohio Industrial Commission has adopted a revised medical and surgical fee schedule, effective May 1, after a series of conferences with the committee on workmen's compensation of the Ohio State Medical Association and a similar committee of the Ohio State Dental Society. A new rule on physical therapy was inserted stating that fees for physical therapy will not be approved for more than ten treatments unless authorized. Under the old rule, fees for such treatment were not allowed unless the treatment was authorized in advance by the commission. The period of after-care covered by a flat fee in surgical procedures, dislocations, fractures, amputations and ophthalmologic procedures was reduced from ninety days to sixty days. This means that additional fees may be paid for services in extended cases—services required after sixty days. A period of three weeks was established as the period covered by the flat fee in ear, nose and throat surgical procedures. The fee for treatment at office after the first treatment was increased from $1.50 to $2, and the fee for treatment at the hospital after the first treatment was increased from $2 to $2.50. Fees were increased in eleven surgical procedures, in six items involving dislocations, in seventeen procedures involving fractures, in five types of amputations, for five ophthalmologic procedures, for two ear, nose and throat procedures and for three x-ray items. The fee for administration of anesthesia in prolonged operations was increased. Under the new schedule the anesthetist is allowed a fee of $10 for the first thirty minutes or fraction thereof and an additional $5 for each succeeding thirty minutes or fraction thereof. The old fee was $10 regardless of the time consumed by the operation. A new item was inserted in the schedule providing a fee of $3 for affidavits furnished by the physician on request of the commission and containing information used as a basis for adjudication of the claim. An entirely new section was inserted in the schedule entitled "Reconstructive Surgery." Such cases (mostly difficult orthopedic and reconstructive surgical cases) must have the authorization of the commission. The schedule provides for six months' after-care under a flat fee which includes the cost of the first cast.

PENNSYLVANIA

District Meeting.—The Tenth and Eleventh Councilor Districts medical societies held their annual meeting at the Penn-Albert Hotel, Greensburg, June 21. Among the speakers were:

Dr. George W. Ramsey, Washington, Facts Regarding the Rh Factor.
Dr. Howard G. Schleiter, Pittsburgh, Identification of Certain Forms of Heart Disease.
Dr. William Bates, Philadelphia, Segmental Pain Suggesting Visceral Disease.
William S. Livengood Jr., Harrisburg, Governmental Paternalism and Inefficiency.

A feature of the meeting was the presentation of testimonials to members who have completed fifty years of practice by Dr. William L. Estes Jr., Bethlehem, president-elect of the state medical society. Those honored included Drs. Albert H. Aber, Dravosburg; Francis J. Madden, Duquesne; Thomas G. Simonton, Pittsburgh; John D. Singley, Pittsburgh; William J. K. Snyder, Avalon; Nathan J. Weill, Pittsburgh; John M. Davis, Darlington; Milton L. McCandless, Rochester; John B. Lowman, Johnstown; Bryant E. Sankey, New Castle; Kate W. Leatherman, Greensburg; Mary L. Montgomery-Marsh, Mount Pleasant, and Harry J. Stauffer, Jeannette.

Philadelphia

Personal.—James P. Lackey, Ph.D., has been named editor of the undergraduate subjects in the sciences for the Blakiston Company.

Fiftieth Anniversary of Laboratory.—On May 20 the laboratory of the Philadelphia Department of Health observed its fiftieth anniversary. Features included a broadcast over WPEN May 19 and an open house the following day.

Dr. Schaeffer Receives Strittmatter Award.—The 1944 Strittmatter award was presented to Dr. Jacob Parsons Schaeffer, professor of anatomy at Jefferson Medical College of Philadelphia, during a special meeting of the Philadelphia County Medical Society May 16 "in recognition of his long and distinguished career as a teacher, author and scientist in the field of anatomy and his sincere and untiring devotion and constructive efforts to safeguard high standards of medical research." This is the twenty-second presentation of the award, which consists of a gold medal and scroll and was made possible in 1923 through the generosity of Dr. Isidor P. Strittmatter. The DaCosta Oration was presented on this occasion by Col. James Barrett Brown, M. C., on "Plastic Surgery in the Military Service."

RHODE ISLAND

Pawtucket Society Observes Fiftieth Anniversary.—On June 6 the Pawtucket Medical Association observed its fiftieth anniversary with a day's celebration at the Pawtucket Golf Club.

Dr. Mowry Retires as Treasurer.—Dr. Jesse E. Mowry, Providence, has retired as treasurer of the Rhode Island Medical Society, concluding twenty-two years' service in the position. Dr. Mowry was president of the Providence Medical Association in 1903, delegate to the American Medical Association in 1916-1917 and president of the Rhode Island Medical Society in 1920.

State Medical Election.—New officers of the Rhode Island Medical Society include Drs. Herman C. Pitts, Providence, president-elect; John F. Kenney, Pawtucket, president; Joseph H. Ladd, La Fayette, vice president; Charles J. Ashworth, Providence, treasurer; Alfred L. Potter, Providence, assistant secretary, and George Raymond Fox, Pawtucket, assistant treasurer. Dr. William P. Buffum, Providence, is secretary.

Surgical Plan Committee Named. — The state medical journal announces a new eleven member committee of physicians and laymen who will study voluntary programs to provide for prepaid medical and surgical insurance similar in operation to the Blue Cross Plan. Lay members of the new committee elected by the six physicians previously chosen by the house of delegates of the state medical society include:

Roderick Pirnie, Providence, insurance executive and state director of the War Finance Committee.

George C. Davis, Providence, lawyer and a member of the board of directors of the Blue Cross.

Charles H. Baker, Providence, head of the industrial firm of Charles H. Baker, Inc.

Ralph Kenyon, Pawtucket, president of the Pawtucket Institution for Savings and a member of the board of trustees of Memorial Hospital.

Harold L. Amrhein, Woonsocket, vice president of the American Paper Tube Company and a trustee of Woonsocket Hospital.

The physicians are Drs. Samuel Adelson, Newport; Hartford P. Gongaware, Westerly; Leo V. Conlon, Woonsocket; George Raymond Fox, Pawtucket, and Herman C. Pitts and Arthur E. Martin, Providence. Dr. Pitts is chairman of the new committee and John E. Farrell, executive secretary of the state medical society, is secretary. Present plans call for a complete review of distribution of medical and surgical services in Rhode Island and also a study of existing medical service plans in other parts of the country that might be adaptable to Rhode Island. The state journal, in its announcement, stated that in the final day of the legislative session the general assembly passed in concurrence an act providing for the incorporation of nonprofit medical service corporations and defining their powers.

TENNESSEE

Waller Leathers Retires.—Dr. Ernest W. Goodpasture, since 1924 professor of pathology, and also associate dean, Vanderbilt University School of Medicine, Nashville, has been appointed dean to succeed Dr. Waller S. Leathers, who will retire June 30. Dr. Sam L. Clark, professor of anatomy at the medical school, has been named associate dean, and Dr. William W. Frye, associate professor of preventive medicine and public health, has been designated professor and head of the department of preventive medicine and public health. The announcement concerning these changes was made during a meeting of the university's board of trust. Dr. Goodpasture received his A.B. in 1907 at Vanderbilt University and graduated at Johns Hopkins University School of Medicine, Baltimore, in 1912. He has been associated with the school since 1924, following years of service at institutions that included Johns Hopkins, Harvard and the University of the Philippines. Dr. Leathers, who graduated at the University of Virginia Department of Medicine, Charlottesville, Va., in 1895, has been dean of Vanderbilt school of medicine and head of the department of preventive medicine and public health since 1928.

UTAH

Personal.—Dr. David C. Budge, medical director of the William Budge Memorial Hospital, Logan, since it was organized in December 1914, has resigned. Dr. Scott M. Budge, associate medical director, was named to succeed him. The latter has been succeeded as associate medical director by Dr. Oliver Wendell Budge. —— Dr. Clay B. Freudenberger, professor and head of the department of anatomy, University of Utah School of Medicine, Salt Lake City, is spending the spring quarter as visiting professor of anatomy at the Louisiana State University School of Medicine, New Orleans.

VERMONT

The Osler Lectures. — Dr. Wesley Bourne, lecturer in pharmacology, McGill University Faculty of Medicine, Montreal, will deliver the Osler Lectures at the University of Vermont College of Medicine at the Fleming Museum, Burlington, July 5-7. His subject for the three lectures will be "Anesthesia: Some Contemplations."

WASHINGTON

New Building for Blood Bank.—Plans will soon be completed for construction of a $100,000 one story reinforced concrete building in Seattle to house the central blood bank (THE JOURNAL, Aug. 5, 1944, p. 982). The project will be financed by contributions, which already total $150,000, to cover construction, equipment and maintenance for a limited period. The blood bank was established a year ago by contributions from twenty business men under the inspiration of Mr. Emil G. Sick, according to *Northwest Medicine*. The land for the blood bank was donated by Dr. Simon Maimon Samuels, Seattle.

Portrait of Physicians.—A portrait of Drs. Walter C. Woodward and Homer D. Dudley, Seattle, was unveiled at the Rainier Club during a dinner meeting of the Seattle Surgical Society and the Puget Sound Surgical Society, April 27. The portrait was presented by the Seattle Surgical Society to the King County Medical Society, May 7, and will be hung permanently with portraits of other physicians in the society's rooms at the Medical-Dental Building auditorium. For the past fifteen years the surgical group has presented an annual two day program, one half of which was serious. The other half is a "high jinks" consisting of a script written and directed by Dr. Woodward and Dr. Dudley and usually devoted to "take-offs" on characteristic traits of their fellow physicians, according to the Seattle *Times*. The portrait shows the two physicians in informal pose and is the work of Neale Ordayne, formerly of Seattle and now located in Texas.

WEST VIRGINIA

Advisory Committee for Legislative Interim Committee.—Governor Clarence W. Meadows has appointed eight physicians as members of an advisory committee which is being set up under the provisions of a concurrent resolution (H. C. R. 4) adopted by the legislature for the purpose of consulting with a legislative interim committee in an investigation and study of public health problems in West Virginia (THE JOURNAL, May 5, p. 44). Members of the advisory committee are Drs. Delivan A. MacGregor, Wheeling; Edwin A. Trinkle, Weston; George O. Martin, Martinsburg; Newman H. Dyer, Bartley; Robert J. Wilkinson and Ray M. Bobbitt, Huntington; Richard O. Rogers, Bluefield, and George F. Grisinger, Charleston.

GENERAL

National Farm Safety Week.—July 22-28 has been designated the National Farm Safety Week, according to Presidential proclamation.

Safety Council Seeks Editorial to Reduce July Fourth Accidents.—An award of $200 for a Fourth of July editorial to help cut down the Fourth of July accident toll is announced by the National Safety Council.

Twenty-Five Years of Hospital Progress.—The twenty-fifth anniversary of *Hospital Progress*, the official journal of the Catholic Hospital Association of the United States and Canada, was observed with its May issue.

Activity Group Therapy for Children.—A training institute in activity group therapy for children will be conducted in New York City under the direction of the American Group Therapy Association. Additional information may be obtained from the association, 228 East Nineteenth Street, New York 3.

Louis Dublin Returns to Metropolitan.—Louis I. Dublin, Ph.D., second vice president and statistician of the Metropolitan Life Insurance Company, has completed his assignment as full time assistant to Basil O'Connor, chairman of the American Red Cross, and as chairman of the organization's administrative committee and has resumed his activities with the insurance company. Dr. Dublin will continue to assist Mr. O'Connor in the long-term policies and plans of the Red Cross and will be active in relation to the operation of the New York City chapters.

Chemical Awards.—The American Chemical Society has awarded the $1,000 Eli Lilly & Company prize for research in biochemistry to Max A. Lauffer Jr., Ph.D., associate professor of physics at the University of Pittsburgh, and the $1,000 Borden Company prize for research in the chemistry of milk to Ben H. Nicolet, Ph.D., senior chemist of the bureau of dairy industry, U. S. Department of Agriculture, Beltsville, Md., the New York *Times* reported June 3. Dr. Lauffer, a former associate at the Rockefeller Institute for Medical Research, was cited for "significant contributions to the study of the physical chemistry of viruses, the kinetics of virus protein denaturation, and the size and shape of macromolecules." Dr. Nicolet was cited for fundamental chemical investigations in the chemistry of milk proteins.

Life Insurance Fund Proposed for Research.—Plans to establish a life insurance fund that would advance more than $500,000 each year for the promotion of medical research were disclosed May 31 by Mr. M. Albert Linton, Philadelphia, chairman of a joint committee of the American Life Convention, Chicago, and the Life Insurance Association of America, New York, according to the New York *Times*. The funds at first would be devoted to diseases of the heart and arteries, it was stated. Foundation grants in 1940 for research into this group of diseases amounted to only 17 cents per

death from these causes against $2.18 per death in cancer, the *Times* states. The life insurance medical research program is to support existing research rather than to establish new research centers. It proposes to extend grants to institutions equipped for research in the chosen field and support carefully selected men who had completed their medical studies and shown special ability in research. Most of these men are now in the armed forces and unless they are helped they may turn to other fields. The new project proposes to assign them as research associates with experienced men already working on cardiovascular diseases.

Science Talks Feature Symphony Intermission.—Edwin J. Cohn, Ph.D., professor of biochemistry, Harvard Medical School, Boston, on May 27 gave the first in a new series of science talks which now feature the intermission of the New York Philharmonic program sponsored by the U. S. Rubber Company. Dr. Cohn's subject was "Blood and Blood Derivatives." The theme of the series is "Science Looks Forward" and the talks in the current group include:

Philip R. White, Ph.D., associate in the department of animal and plant pathology, Rockefeller Institute, Princeton, N. J., Roots, Nerves and Kidneys, June 3.
Charles K. Leith, Sc.D., head of the metals and minerals branch, Production Research and Development, War Production Board, Madison, Wis., Metals in War and Peace, June 10.
Robert M. Yerkes, Sc.D., professor of psychobiology, Yale University School of Medicine, New Haven, Conn., Chimpanzees as Servants of Science, June 17.
Henry N. Russell, Ph.D., research professor of astronomy, Princeton University, Princeton, N. J., Are the Other Planets Habitable? June 24.
John G. Kirkwood, Ph.D., Ithaca, N. Y., associate editor of the *Journal of Chemistry and Physics*, What Is a Liquid? July 8.
Isaiah Bowman, LL.D., president, Johns Hopkins University, Baltimore, The New Geography, July 15.
Dr. George R. Minot, Boston City Hospital, Anemia, July 22.
George R. Harrison, Ph.D., professor of physics, Massachusetts Institute of Technology, Cambridge, Atoms, July 29.
Robert C. Murphy, Sc.D., zoology, ornithology, American Museum of Natural History, New York City, subject not announced, August 5.
George B. Cressey, Ph.D., geology, geography, Syracuse University, Syracuse, N. Y., Our Northern Neighbor, China, August 12.
Charles E. K. Mees, Sc.D., director of research and development of the Eastman Kodak Company, Rochester, N. Y., Cows, Movies and Color Photography, August 19.

The Lasker Awards for Fertility Research and Maternal Care.—The Planned Parenthood Federation of America announces two $500 Lasker Awards for significant contribution to the improvement of maternal health care and for research in human fertility. The awards will be given to the scientist making the most significant contribution in research in human fertility, either in the control of conception or in the correction of infertility and to the public health service in a state or community for meritorious action in developing a complete program of maternal health care, including child spacing. The individual recipient of the award will be the executive officer most responsible for the development of the program. The fertility award will be given in honor of the late Dr. Hannah M. Stone, first medical director of the Margaret Sanger Research Bureau. The public health award will be in honor of Mrs. Margaret Sanger, founder of the birth control movement and at present honorary chairman of the federation. The awards will be presented at the annual dinner of the Planned Parenthood Federation of America in New York in January 1946. Deadline for submission of entries for the awards will be December 1. Two similar awards were presented last January to John MacLeod, Ph.D., of the department of anatomy, Cornell University Medical College, New York, and to Dr. Felix J. Underwood, Jackson, Miss., executive officer of the Mississippi State Board of Health. Any individual wishing to qualify for the awards or to suggest the name of a scientist, physician or public health official who might do so should address the medical committee, Planned Parenthood Federation of America, 501 Madison Avenue, New York 22.

Special Committee to Study New Approach on Cancer.—A special committee on growth consisting of fourteen experts has been appointed at the request of the American Cancer Society and in cooperation with the division of medical sciences of the National Research Council to project an "unprecedented approach" to the cancer problem. Authorities from fields as scattered as plant biology and genetics agreed to consolidate their information and plans in one organization, which will in turn encourage research through widespread grants of merited fellowship. The approach differs from all others heretofore in that cancer sometimes has been regarded as a distinct field, a tendency which many experts regard as a fallacy. The new program will attempt to advance the basic knowledge about cancer as well as encourage the fuller usage of what is known already, although in this second respect considerable gains are being made. The committee on growth will seek "to support institutions and individuals whose research work is related to finding new methods of treating cancer." Other objectives will be:

To make grants of such magnitude that individual researchers will be able to appoint subordinates for long training periods.
To arrange for the economic long-range security of researchers interested in the field.
To arrange for conferences of competent groups to interchange reports.
To make surveys to analyze the problems and progress relating to cancer.
To initiate and plan broad or specific programs of research.

The committee on growth expects some of the later nominees for fellowships to be men currently in the armed services. Rather than make the selections itself, the National Research Council will designate certain institutions with whose activities it is familiar, to make the awards in turn. Just as the committee membership has not been limited to cancer specialists, the research council pointed out the fellowships would be available to a diversity of candiates, in even such fields as engineering. Funds for research will come from the $5,000,000 campaign which has been under way recently. Members of the executive committee include Dr. Cornelius P. Rhoads, medical director of Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York; Clarence C. Little, Sc.D., Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine; Dr. James B. Murphy, Rockefeller Institute for Medical Research, New York, and Dr. Milton C. Winternitz, Yale University School of Medicine, New Haven, Conn. Others on the committee on growth are:

Dr. Alphonse R. Dochez, Columbia University College of Physicians and Surgeons, New York.
Dr. A. Baird Hastings, Harvard Medical School, Boston.
Dr. Charles B. Huggins, University of Chicago.
Donald F. Jones, Sc.D., Connecticut Agricultural Experiment Station, New Haven.
Carl R. Moore, Ph.D., University of Chicago.
Dr. John J. Morton Jr., University of Rochester School of Medicine and Dentistry, Rochester, N. Y.
Dr. Eugene P. Pendergrass, University of Pennsylvania School of Medicine, Philadelphia.
Dr. Florence R. Sabin, Denver.
Dr. Howard C. Taylor Jr., Bellevue Hospital, New York.
Merle A. Tuve, Ph.D., Johns Hopkins University, Baltimore.

FOREIGN

Albert Szent-Györgi in Moscow.—Dr. Albert Szent-Györgi, professor of medical chemistry, Szeged University, Szeged, Hungary, who won the Nobel Prize in 1937 for his work with vitamin C, is reported to have arrived safely in Moscow from Budapest, according to the New York *Times*. It was stated that the Swedish legation in Budapest managed to save Professor Szent-Györgi from the Nazis by employing him as a chauffeur.

Egypt Approves Birth Control.—The Grand Mufti of Egypt, highest judicial authority under Moslem religious law, has sanctioned the practice of contraception in marriage under a wide variety of circumstances ranging from ill health to economic hardship. The approval was contained in a "fatwa," or judgment, which also permits abortion prior to the "quickening of the embryo" in cases in which the life of the mother, the "prospective child" or a child already born may be threatened. The announcement of the sanction was released through the Planned Parenthood Federation of America, New York.

Death Rate Increases.—During the four week period starting March 1 the death rate in Amsterdam was three times as high as during the corresponding period in 1939, according to the Netherlands Information Bureau. The very young and the very old whose resistance had been lowered by years of undernourishment were the groups hardest hit. The report indicates that there has been considerable increase in communicable diseases. Diphtheria, which in prewar years showed a rate of 400 to 600 annually, assumed epidemic proportions during 1944, when 7,800 cases were reported in Amsterdam alone. From 20,000 to 30,000 persons were found to be suffering from hunger edema, while tens of thousands of others were at the brink of starvation, it was stated. Netherlands health authorities were startled by a report from the chief of Allied Supreme Headquarters public health branch that "health conditions in Holland were not as bad as expected." The statement at SHAEF by Major General Warren F. Draper, U. S. Public Health Service, declared that the special feeding teams that had been alerted for action "were not needed." In reply to this, Dutch health authorities who had just returned from an eye witness tour of the western provinces declared that even two weeks after liberation people were still dying of starvation, while many were too weak even to reach the new distribution centers. Far from being "not needed," the twenty-nine feeding teams operating in the western provinces have been increased to forty-three. Eight of these teams are operating in Amsterdam, four in The Hague, six in Rotterdam and the others in various towns where large numbers of starvation victims have been found.

Foreign Letters

LONDON

(From Our Regular Correspondent)

May 19, 1945.

The British Council of Rehabilitation

As shown in previous letters to THE JOURNAL, war injuries have led to the concentration of attention on the problem of rehabilitation. A British Council of Rehabilitation has been established (1) to act as a coordinating center for the various interests concerned in the widest aspects of rehabilitation, (2) to promote and correlate courses of study, (3) to invite the active cooperation of government departments, hospitals, universities, training colleges, educational institutions and research foundations in promoting the study and practice of rehabilitation, (4) to secure the active cooperation and participation of commerce, industry and professional bodies in the problems of resettlement, (5) to encourage the formation of follow-up schemes for the rehabilitated and (6) to consider, promote or oppose legislation which may affect the interests of the disabled and to make such representations as may be desirable. The council will comprise two representatives from each of its member organizations, elected members and such others as the council may from time to time appoint. The member organizations are the Association of Industrial Medical Officers, the Association of Occupational Therapists, the Board of Registration of Medical Auxiliaries, the British Federation of Social Workers, the British Hospitals Association, the British Legion, the British Medical Association, the British Orthopedic Association, the Central Bureau for Insurance Nursing, the Central Council for the Care of Cripples, the Chartered Society of Physiotherapy, the Industrial Orthopedic Society, the Institute of Labor Management, the Miners Welfare Commission, the National Association for the Prevention of Tuberculosis, the National Institute for the Blind, the National Institute for the Deaf, the National Institute of Industrial Psychology and the Research Board for the Correlation of Medical Science and Physical Education.

Accidents from Gas Cylinders Used with Anesthetic Apparatus

The serious risk that the pipe line used with anesthetic apparatus may in error be connected with the wrong cylinder, e. g. to a cylinder containing nitrous oxide instead of oxygen, has led the Ministry of Health to send a circular to hospitals. A number of fatal accidents have occurred. The minister of health is advised that where it is the practice for any person other than the anesthetist to replace gas cylinders on anesthetic apparatus or to connect such apparatus to a pipe line installation, the risk of accidents would be minimized if arrangements were made for a second person, preferably a doctor, to examine the connections to ensure that a mistake has not been made. It is suggested that the person responsible for the examination might on each occasion also be required to make a note of the fact by signing a record book especially kept for the purpose.

The Treatment of Starvation Under the Germans

The treatment of cases of advanced starvation in German concentration camps and in occupied countries robbed of their food supplies, especially the Netherlands, is a grave problem. Impressed with the evidence of the value of hydrolysates for alimentation by the intravenous or oral route, the military authorities are providing this treatment. They are also testing the efficacy of plasma and serum, which have been supplied from the Lister Institute in large quantities. Glucose is also given in large quantities to spare the amino acids for purposes of repair, and vitamins. The results are not yet available.

A less serious problem was that of Dutch children, aged 7 to 15 years, brought to England from the Netherlands. They had been living for a long time on bread, potatoes and cabbage. They did not appear much wasted but were undersized. The extent to which they were underweight is shown by the fact that they gained up to 6 pounds 6 ounces (2,900 Gm.) in three weeks on a proper diet. But in the starvation areas of the Netherlands there are children whose diet has fallen to 300 calories a day and who will present a more serious problem.

English Books to Be Translated and Produced for Russia

An agreement has been signed at the Soviet embassy in London between Mezhdunarodnaya Kniga of Moscow and Hutchinson, the English publisher, by which the former will distribute Russian translations of English books. These books will be translated and produced in England by the English publisher and exported to Russia. The agreement will hold for a minimum period of three years. The books to be translated have not yet been announced, but no doubt medical books will figure largely among them. This is further evidence of the looking of the European nations to London for a lead after the war and the desire that the British capital should succeed to the hegemony formerly held by Berlin, which were mentioned in previous letters to THE JOURNAL.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, May 2, 1945.

The Sanitation Projects of the Amazon and the Rio Doce

Dr. George C. Dunham, director of the medical division of the Bureau of the Coordinator of Inter-American Affairs, recently spent a few days in Brazil to inspect the work of some of the projects of the Special Service of Public Health (the SESP, as it is called in Brazil), a medical organization run in cooperation by the governments of the United States and Brazil. Dr. Paulo Antunes is the director of the Amazon project, with headquarters at Belem, state of Pará, and Dr. Ernani Braga is the director of the Rio Doce project, with headquarters at Vitoria, state of Espirito Santo. Dr. H. V. Markham, director of the Central Hospital at Belem, and two more doctors are the only Americans at present connected with the two projects, the rest of about 3,000 officials and workers being Brazilians. Almost 50 Brazilian physicians are now studying in the United States, through fellowships awarded by the Institute of Inter-American Affairs, to work, after their return, in the two projects. The Schools of Nursing of São Paulo and Belem are training more than 50 young women to be used as nurses in the same work. In the vast region of the Amazon basin, where rivers are almost the only means of communication, many scattered treatment stations have been established for the campaign against malaria. Small steamers and launches are used to transport doctors, nurses and other workers, some of these small vessels being employed as mobile clinics. Several district laboratories have been established, where simple entomologic work is performed in coordination with the central laboratory at Belem, Pará. The International Health Division of the Rockefeller Foundation transferred to the SESP its specialized personnel who had been previously used in the campaign to eradicate the anopheline Gambiae imported from Africa, as well as an important bulk of equipment suitable to this kind of work. Since August 1942 the Institute Evandro Chagas of Belem, a branch of the Oswaldo Cruz Institute of Rio de Janeiro, has been closely cooperating in the Amazon project, with a modern hospital, a great laboratory and a training school. There are other hospitals at Manaos, Breves and Santarem, which are the principal cities of this section of the country.

Treatment of Pulmonary Tuberculosis with Thoracoplasty

Dr. Eduardo Etzel of the Vicentina Aranha Sanatorium at São José dos Campos, state of São Paulo, has just published a report on 122 consecutive cases of pulmonary tuberculosis treated with thoracoplasty. In 22 cases the treatment was not completed. Dr. Etzel points out the futility of attempting the thoracoplasty in patients whose pulmonary condition does not permit a good surgical collapse. Of the 100 cases in which the treatment was completed, there were unilateral lesions in 65 and bilateral lesions in 35. In the first group, 57 cases were cured, or 87.6 per cent. Etzel believes that the minimum period of six months is absolutely necessary to appraise the good results of thoracoplasty. The poor results in the 8 unilateral cases were caused by late hematogenic dissemination (1), by contralateral postoperative dissemination (1), by tracheobronchial tuberculosis (2), by residual tuberculous process (2), by residual cavity (1) and by secondary open cavity (1). In the group of bilateral cases 19, or 54.2 per cent, were cured. The poor results in the 16 bilateral cases were caused by contralateral cavity (7), noncavitary extensive fibrous lesions (3), contralateral pneumothorax with cavity (2), contralateral pneumothorax and residual cavity (2), contralateral pneumothorax with exudative lesions (1) and contralateral exudative lesions (1). A careful selection of cases must be made to determine the efficiency of the respiratory function, to avoid the operation on patients who may later present chronic dyspnea, causing permanent infirmity and even death. The stability of the lesion that has to be collapsed and the degree of fibrosis or the degree of productive reaction must be taken into consideration, as thoracoplasty is contraindicated in cases in which there are progressive and "soft" lesions without fibrous reaction. In cases with bilateral involvement the thoracoplasty must be performed only if the contralateral lesions are regressive, arrested or controlled through pneumothorax. Tracheobronchial tuberculosis is a contraindication to thoracoplasty if the disease is advanced or bilateral. In case of fibrous stenosis of a main bronchus, dilation is necessary before the thoracoplasty. In cases of tracheobronchial tuberculosis treatment of the pulmonary lesion must be performed first.

Brief Items

Dr. Pasteur Valéry-Radot of Paris, head of the French cultural mission to South America, is now in Rio de Janeiro. At the Medical School of the university he delivered a lecture on "French Medicine During the War."

Dr. George K. Strode, director of the International Health Division of the Rockefeller Foundation, spent a number of days at Rio de Janeiro, where he was invited to attend a special meeting held by the Brazilian Society of Hygiene in his honor and a luncheon, during which he was greeted by Dr. Afranio Peixoto, professor emeritus of hygiene at the Rio de Janeiro University. Dr. Strode was the head of the staff of the International Health Division in Brazil from 1921 to 1926.

A model health center has been inaugurated at Petropolis, the summer capital of Brazil (population 40,000). The building has been erected by the federal government and equipped by the state of Rio de Janeiro to be used as a training center for health officers and for public health nurses as well as a special demonstration of modern public health administration. The director of the center, Dr. Oswaldo L. Da Costa, has a diploma in public health from the Johns Hopkins University.

Dr. Francisco Gugliotti has been appointed director of the Hospital São Sebastião of Rio de Janeiro, the institution in which the acute cases of transmissible diseases are isolated.

The Legião Brasileira de Assistencia is now building a hospital for tuberculous children at Fortaleza, state of Ceará.

Dr. Antonio Murtinho Nobre, a practitioner of medicine in the city of São Paulo, died at Rio de Janeiro, aged 66.

MEXICO

(From Our Regular Correspondent)

MEXICO CITY, May 25, 1945.

United States Physicians Excluded

United States physicians are virtually excluded from practicing in Mexico under the terms of a new and rigid federal law designed to eliminate foreign influences from the Mexican scientific professions. The legislation, which was announced on May 26 by publication in the *Official Daily*, a government organ, took effect two days later. Although it lays down a complete system of control for a number of professions, the most important section of the law, as far as doctors of the United States are concerned, is that declaring "no foreigner can practice, in the Federal District and territories, the scientific professions covered by this law." The medical profession is specifically named as one of the fields which have been closed to foreigners. Nevertheless, government sources indicated that physicians already practicing here will probably not be affected. While this point has not as yet been clarified by an official legal opinion, it is reported that such practitioners, who constitute some of the country's leading medical authorities, will merely be required to register their qualifications with the General Bureau of Professions, the government agency which will administer the legislation. Another exception will be made for refugee physicians, who, the statute provides, will be conceded "temporary permits" to practice, provided they are able to "prove themselves to be the victims of political persecution in their own country." Further exemptions will be granted to "professors of specialties still not taught (in Mexico)" or to those "who display unquestionable and outstanding competence," to "consultants or instructors dedicated to the establishment, organization or installation of institutions of public or military instruction, laboratories or institutes of essentially scientific character" and to "technical directors." Following is a partial text of the law:

"No foreigner can practice, in the Federal District and territories, the scientific professions covered by this law.

"Naturalized Mexicans who have conducted all their studies in authorized higher institutions can enjoy the same privileges of professional practice as Mexicans by birth.

"Only in exceptional cases can the General Bureau of Professions, in agreement with the respective institutions and in accordance with legal requisites, grant temporary permission to practice to foreign professional men and women, resident in the Federal District and territories, who prove themselves to be victims of political persecution in their own country.

"Degrees issued abroad to Mexicans by birth can be registered with the Ministry of Education, provided the course of studies leading to the professional degree is the same as or similar to those in institutions recognized by the Mexican government.

"In cases where it is impossible to establish the similarity of the studies, a system of examination will be set up to subject candidates to tests to prove their training.

"Foreigners and naturalized Mexicans who possess a degree in any of the professions embraced by this law must:

"1. Be professors of specialties still not taught or display unquestionable and outstanding competence in the opinion of the General Bureau of Professions.

"2. Be consultants or instructors dedicated to the establishment, organization or installation of institutions of public or military instruction, laboratories or institutes of essentially scientific character.

"3. Be technical directors in the development of the country's natural resources.

"The activities authorized for foreigners and naturalized Mexicans in the foregoing will in any case be temporary.

"The Ministry of the Interior will authorize the entry of foreign professional men and women into national territory, subject to the preceding conditions."

BUENOS AIRES

(From Our Regular Correspondent)

May 24, 1945.

Preventive and Curative Medicine

A law was recently passed giving the Instituto Nacional de Previsión Social charge of administering preventive and medical care to workers and employees who are protected by social insurance. Special attention will be given to patients with chronic diseases of great social importance, such as tuberculosis, cardiovascular diseases, syphilis, rheumatism, industrial diseases and their complications, as well as to industrial invalidism and physical and technical readaptation of workers after illness or accidents. The institute will carry out periodic examination of socially insured workers. No insured worker will be allowed to go without examination for more than one year. An individual clinical record book will be prepared and filed. Workers who are in need of rest will be instructed to reduce the number of working hours or to discontinue work for a certain time. Employers must give workers necessary rest or even a leave of absence for six consecutive months. Employees who are taking a partial or complete rest period will obtain a portion of the regular salary from the employer and the remainder from the Instituto Nacional de Previsión Social. A certain amount will be given to socially insured workers with illness of more than six months' duration. On returning to work an employee is to be given his former job with the regular salary or work better suited to his physical or mental capacity as determined by the institute. Retired invalids are given hospitalization up to a period of not more than six months. When expenses of hospitalization of retired invalids last for several months, 20 per cent of the allowance given to retired workers with a family and 50 per cent of the allowance of retired workers without any family is applied to the expenses of hospitalization. The insured are to obey medical orders. They are not allowed to work with or without payment during a treatment of preventive or curative rest. A budget will be prepared within two years in accordance with expenditures. An insured person is to pay 2 pesos ($0.50) every year for his general medical examination.

Congress of Ophthalmology

The second Pan American Congress of Ophthalmology will be held in Montevideo in November. The officers of the congress are Dr. H. S. Gradle of Chicago, president, Dr. Alberto Vázquez Barrière of Uruguay and Dr. Francisco Belgeri of Argentina vice presidents and Dr. Moacyr E. Alvaro of Brazil executive secretary. At a recent congress in Buenos Aires it was resolved to hold the second congress on Nov. 26, 1945 in Montevideo. Subjects on the program include diagnosis and therapy of preglaucoma, gonioscopy in view of newer knowledge of glaucoma, evaluation and mechanism of destructive effects of ocular hypertension, need of early operation in glaucoma, duration of medical therapy in glaucoma surgery of paralytic strabismus and surgery of heterophoria and concomitant strabismus. Two new topics, contact lenses and gonioscopy, appeared in the most recent program. These subjects will be presented by Drs. Baudilio Courtis of Buenos Aires and H. S. Sugar of Detroit and will be discussed by Drs. D. G. Cogan of Boston and A. Urretz Zavalia of Cordoba. Dr. Alberto Vázquez Barrière of Uruguay will preside. The session on prevention of war will open on the afternoon of November 26. Dr. Francisco Belgeri will preside. Dr. Correa Mayer of Porto Alegre will preside over the session on trachoma.

Dr. Gradle of Chicago recently stated that no ophthalmologic or other scientific news can be reported from Europe because of war conditions. The progress of ophthalmology rests with American centers. Postgraduate studies of the specialty are now receiving proper attention. The Kellogg Foundation offers twenty-five fellowships for postgraduate studies. The second Pan American Ophthalmologic Congress will be a scientific event of great importance to Pan American ophthalmologists. Probably more than one hundred and fifty American ophthalmologists will attend the congress.

Cinematographic Medical Films

Cinematographic equipment was recently obtained by the library of the Faculty of Medicine of the University of Buenos Aires for the purpose of illustrating certain chapters of medicine by means of films. The faculties of medicine as well as other scientific and educational centers of the country will receive copies of the names of the films which are available from the National Center Archivo Gráfico. The films requested from the Archivo Gráfico may be kept at the given educational center as long as they are needed. An apparatus providing the proper phonographic records for the film is lent with the film.

Electrocardiographic Action of Mate Tea

Dr. Enrique Moisset de Espanés recently reported to the Sociedad de Biología of Cordoba the results of electrocardiograms of 15 young men which were taken after ingestion of tea made from 200 Gm. of mate leaves. In the majority of the subjects the voltage of the electrocardiogram increased, especially in the T and R waves and moderately in the P wave. The increase of the voltage persisted in electrocardiograms which were taken one hour after ingestion of the tea.

Control of Exportation of Drugs

A law was recently enacted by the government of Argentina to the effect that custom houses will not permit exportation of drugs without the authorization of the National Department of Public Health. Permits will be issued only when the national needs for the drug in question have been satisfied. Production of certain drugs to be exported will be authorized by the National Department of Health.

Personal Items

Dr. Aloysio de Castro of Rio de Janeiro was recently invited to visit the medical societies of Buenos Aires. The Ateneo de la Historia de la Medicina held an extraordinary meeting in honor of Dr. de Castro, who was appointed honorary member of the academy. Dr. Castro presented to the academy a bust of Dr. Oswaldo Cruz which was made and given by Dr. Phocion Serpa of Rio de Janeiro, and Dr. Castro also awarded to some Argentine members of the academy the diplomas of honorary membership in the Sociedad Paulista de Historia de la Medicina.

Marriages

Robert Jackson Wetmore, Durham, N. C., to Miss Jane Carlton Evans of Washington, D. C., in Chevy Chase, Md., May 11.

Reuben L. Chrestman Jr., Memphis, Tenn., to Miss Deanne Henson of Meridian, Miss., in West Memphis, Ark., recently.

Thomas Fitz-Hugh Jr., Wynnewood, Pa., to Miss Bernice Rowe of Philadelphia in Washington, D. C., March 26.

Mary Charlotte Van Gundy, Beverly Hills, Calif., to Mr. Campbell E. Holmes of Los Angeles, April 5.

Henry V. Guhleman Jr., Jefferson City, Mo., to Miss Mary Florence Laws of Snow Hill, Md., April 7.

William Mahon Myers, Philadelphia, to Miss Jane Louise Mather of Latrobe, Pa., March 17.

Bernard Frank Joseph Fetter to Miss Anna Lee Hinton, both of Durham, N. C., May 11.

Carol H. Konhaus, Mechanicsburg, Pa., to Miss Frances M. Flickinger of Harrisburg, April 21.

Herbert S. Hunter, Latrobe, Pa., to Miss Lois Augusta Anderson of Greensburg, April 6.

Charles F. Taylor to Miss Jeanne N. Klinepeter, both of Harrisburg, Pa., April 1.

Deaths

Charles Goodman ⊕ New York; Western Reserve University Medical Department, Cleveland, 1892; formerly clinical professor of surgery at the University of Bellevue Hospital Medical College; fellow of the American College of Surgeons and the New York Academy of Medicine; member and past president of the Harlem Medical Association; past president of the Eastern Medical Society, the Park West Hospital Medical Board and the Beth Israel Hospital Medical Board; first vice president of the International Medical Club; formerly secretary of the Alumni Association of Mount Sinai Hospital; member of the International Surgical Society, Metropolitan Medical Society, American Public Health Association, Physicians' Mutual Aid Association, Military Order of the World War and the Reserve Officers' Association; volunteered and commissioned a captain in the medical reserve corps of the U. S. Army in May 1917; later organized and commanded a reinforcement group for the Presbyterian Hospital unit abroad, which was General Hospital number 1 of the American Expeditionary Forces; after his promotion to major headed an operating team during the British Expeditionary Force Paschendale offensive; later was director of a field hospital section of the Rainbow division of the American Expeditionary Forces and consulting surgeon to other American divisions; honorably discharged in April 1919; lieutenant colonel, medical reserve corps, U. S. Army, not on active duty; director of the typhus research fund of New York University; consultant in vascular surgery, Veterans Administration; in 1936 a member of the Nobel Prize nominating committee in medicine; for twenty years chief of the surgical division of the outpatient department of Mount Sinai Hospital; consulting surgeon and for twenty years attending surgeon at the Beth Israel Hospital; served as attending surgeon at the Montefiore Hospital, Park West Hospital and the Sydenham Hospital; for two years director of surgery and for two years director of vascular surgery at the Broad Street Hospital; consulting surgeon at the Rockaway Beach (N. Y.) Hospital, Home for Daughters of Jacob and the New York Polyclinic Hospital; member of numerous scientific groups and extensive contributor to the literature; credited with performing in 1906 the first successful blood transfusion; died May 23, aged 73, of heart disease.

Richard Slee, Stroudsburg, Pa.; Long Island College Hospital, Brooklyn, 1891; member of the American Medical Association and the Medical Society of the State of New York; in 1908 among the first to be commissioned in the newly created medical reserve corps of the U. S. Army as a first lieutenant; in 1916 he was sanitary officer at the medical officers training camp at Tobyhanna, Pa.; in command of Camp Crane, Allentown, Pa., 1918-1919; on Sept. 7, 1922 organized and served as commanding officer in charge of General Medical Laboratory number 1, Slee Laboratory Unit at Swiftwater; first National Commander of the United States Army Ambulance Service Association, 1920-1921; colonel, medical reserve corps, U. S. Army, not on active duty; first deputy health commissioner of Westchester County, N. Y., from 1930 to Oct. 1, 1937, when he retired; formerly district health officer of the state health department of New York; at one time assistant bacteriologist and medical inspector, Pennsylvania State Health Department; founder of the Slee Antitoxin and Vaccine Laboratories, Swiftwater; died April 8, aged 78, of cerebral hemorrhage.

Philemon Edwards Truesdale ⊕ Fall River, Mass.; Harvard Medical School, Boston, 1898; member of the founders group of the American Board of Surgery; member of the American Surgical Association, New England Surgical Society and the American Association for Thoracic Surgery; fellow of the American College of Surgeons; served as vice president of the Massachusetts Medical Society; joined the medical corps of the U. S. Army in 1917 and sailed for France with the rank of captain in the Yale Mobile Hospital unit; in October 1918 promoted to the rank of major; on his return to the United States assigned as director of surgery at Camp Devens and honorably discharged on March 15, 1919; member of the House of Delegates of the American Medical Association in 1929; awarded a gold medal in 1929 in the Scientific Exhibit of the American Medical Association for exhibit showing experimental demonstration of the mechanism of transposition of abdominal viscera following rupture of the diaphragm; medical director of the Truesdale Hospital, which he had founded and where he died June 12, aged 70.

Charles Johnson Smith ⊕ Portland, Ore.; Starling Medical College, Columbus, 1888; Bellevue Hospital Medical College, New York, 1890; member of the House of Delegates of the American Medical Association in 1905, 1910 and 1911; past president of the Oregon State Medical Society; for two terms mayor of Pendleton; state senator from Umatilla County from 1902 to 1910; for eighteen years a member of the school board of Pendleton; a member of the Industrial Welfare Commission and chairman of the board of curriculums from 1912 to 1930; one of the organizers and past president of the state board of health; fellow of the American College of Surgeons; for eight years Democratic state chairman for Oregon; president of the Ohio Society of Oregon; surgeon for the Western Division of the Northern Pacific Railroad Company; died April 19, aged 80, of angina pectoris.

William Litterer, Miami, Fla.; Vanderbilt University School of Medicine, Nashville, 1901; formerly professor of bacteriology and assistant professor of preventive medicine and public health at his alma mater, director of laboratories for the Tennessee Department of Public Health for many years; member of the American Medical Association, Tennessee State Medical Association, Southern Medical Association, American Chemical Society, Society of American Bacteriologists and the American Association for the Advancement of Science; did special government research in lethal gas during World War I; died May 1, aged 67, of cerebral thrombosis.

Hyman John Rubenstein ⊕ New York; Tufts College Medical School, Boston, 1927; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; Littauer Pneumonia Research Fellow at Harlem Hospital, 1929-1930; served as instructor of otorhinolaryngology at the New York Polyclinic Medical School and Hospital; on the staffs of the Beth Israel and Metropolitan hospitals; consultant to the Home of the Daughters of Israel; formerly on the staffs of the Polyclinic Hospital and the Mount Sinai Hospital, where he died April 30, aged 41, of leukemia.

Earle B. Stokes ⊕ East Orange, N. J.; Jefferson Medical College of Philadelphia, 1914; specialist certified by the American Board of Urology, Inc.; member of the American Urological Association; fellow of the American College of Surgeons; served during World War I; member of the Selective Service System; on the staffs of the Essex County Hospital, Cedar Grove, Essex Mountain Sanatorium, Verona, East Orange General Hospital, Dover (N. J.) General Hospital and the Orange (N. J.) Memorial Hospital, where he died April 29, aged 53, of coronary thrombosis.

Jesse Wolfenden Battershall, Attleboro, Mass.; Tufts College Medical School, Boston, 1916; member of the American Medical Association; since 1925 medical examiner for North Bristol District; served as school physician; since October 1943 health officer; past president of the Medico-Legal Association of Massachusetts and the Doctors Club of Attleboro; director of the Bristol County Health Association; interned at the Robert Brigham Hospital in Boston; on the staff of the Sturdy Memorial Hospital, where he died May 4, aged 51, of embolism following a major operation.

Arnold Frederick Sydow ⊕ Cleveland; Ohio State University College of Medicine, Columbus, 1926; fellow of the American College of Surgeons; demonstrator of surgery at the Western Reserve University School of Medicine; on the staffs of the City and St. Luke's hospitals; physician in charge of the medical staffs at the Cleveland works of the Aluminum Company of America, the Jones and Laughlin Steel Corporation and many smaller Cleveland firms; served on draft board number 30; died in West Palm Beach, Fla., April 28, aged 44, of malignant retroperitoneal tumor.

William Frederick Bennett ⊕ Verona, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; in 1923 joined the Essex Mountain Sanatorium, where since 1928 he served as first assistant physician; formerly on the staff of the Pennsylvania State Sanatorium for Tuberculosis in Hamburg, Pa.; died in the Mountainside Hospital, Montclair, May 2, aged 67, of cerebral hemorrhage and suppurative cholecystitis.

Simon William Brownstein, Chicago; Barnes Medical College, St. Louis, 1899; served during World War I; for eighteen years chief of clinics for the city board of health; died May 7, aged 78, of coronary thrombosis.

Orlo Solomon Canright, Columbus, Ohio; Rush Medical College, Chicago, 1884; died May 1, aged 87, of coronary thrombosis.

Etienne Pascal Crowe, Cleveland; University of Wooster Medical Department, Cleveland, 1889; a founder of the Cleveland Academy of Medicine; until his retirement in 1920 had been medical examiner for the John Hancock Life Insurance Company for thirty years; died May 6, aged 86, of disease of the coronary artery.

John Engelbrecht, Stony Hill, Mo.; Homeopathic Medical College of Missouri, St. Louis, 1893; died March 15, aged 77, of cerebral hemorrhage.

Samuel Wallace Fowler, New York; College of Physicians and Surgeons, New York, 1895; member of the American Medical Association; served as instructor in urology at the Vanderbilt Clinic and at Bellevue College Clinic and also in syphilology at New York Hospital; died March 21, aged 75, of thrombosis.

Harrison H. Hayward, Randolph, Vt.; University of Vermont College of Medicine, Burlington, 1900; member of the American Medical Association; health officer; on the staff of the Gifford Memorial Hospital; died May 12, aged 67, of coronary thrombosis.

George Watson Jacoby, Ashland, Ohio; Ohio Medical University, Columbus, 1905; died May 1, aged 63, of carcinoma between the bladder and the rectum.

Barnet Joseph ✠ New York; Long Island College Hospital, Brooklyn, 1904; at one time laboratory instructor in anatomy and pathology at the University of Vermont College of Medicine, Burlington; a major in the medical corps of the U. S. Army during World War I; co-founder of the city cancer clinic and a representative of the board of health to the London Cancer Conference of 1928; served as head of the tumor service at the Downtown Hospital and at one time director of the Madison Hospital; died May 9, aged 62, of cerebral hemorrhage.

Harry Butler Knapp ✠ Wellsboro, Pa.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1904; fellow of the American College of Surgeons; formerly medical director of the Pocono Nutrition Center at Mount Pocono, Pa.; chief surgeon at the Wellsboro Hospital; died February 22, aged 68, of coronary occlusion.

Edwin Roy Leib ✠ Worcester, Mass.; Boston University School of Medicine, 1899; epidemiologist for the department of public health of Worcester; served during World War I; past president of the Worcester District Medical Society and a councilor for the Worcester District of the Massachusetts Medical Society; consultant on the staff and formerly chief of the medical service at the Hahnemann Hospital; consultant on the staff of the Belmont Hospital; president of the city blood bank for civilian defense; died May 3, aged 69, of coronary thrombosis.

Harry Lazarus Levant ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1905; served on the staff of the Beth Israel Hospital; died in the Hospital for Joint Diseases May 12, aged 62, of metastatic carcinoma.

Frank E. Lock, Buffalo; University of Buffalo School of Medicine, 1897; also a pharmacist; died April 28, aged 74, of myocarditis.

David Hunt Ludlow, Easton, Pa.; Gross Medical College, Denver, 1892; member of the American Medical Association; once assistant professor of mathematics, University of Tennessee; also a lawyer; at one time lecturer on physiology at his alma mater; said to be the inventor of the Ludlow eyeglass guard; a founder member of the Denver Clinical and Pathological Society, serving as its reporting secretary; died April 13, aged 87, of cerebral hemorrhage.

Antonio E. Malavazos ✠ New York; National University of Athens School of Medicine, Greece, 1911; served as a medical officer in the Greek army from 1912 to 1920; assistant visiting physician at the Metropolitan Hospital; clinical assistant at the Polyclinic Hospital and a member of the staff of the Newark Beth Israel Hospital; died April 20, aged 56, of heart disease.

Amon A. Mayfield, Sikeston, Mo.; St. Louis College of Physicians and Surgeons, 1891; member of the American Medical Association; for many years a member of the board of public works; member of the school board; died April 8, aged 77, of heart disease.

Louis Eugene McCanna, Washington, D. C.; George Washington University School of Medicine, Washington, 1916; served during World War I; formerly associated with the U. S. Public Health Service; died in the Veterans Administration Facility, Mount Alto, April 26, aged 54, of coronary heart disease.

Harry Hugo McClellan, Dayton, Ohio; Vanderbilt University School of Medicine, Nashville, Tenn., 1912; served as camp psychiatrist at Macon, Ga., during World War I; formerly superintendent of the Dayton State Hospital; died in St. Elizabeth Hospital May 1, aged 56, of malignant tumor of the brain.

Fred Martin Rankin ✠ Akron, Ohio; Eclectic Medical Institute, Cincinnati, 1919; served as police and fire department surgeon; member of the staff of the City Hospital; died April 17, aged 55, of coronary thrombosis.

Willis Frederick Reinhardt, Hypoluxo, Fla.; Beaumont Hospital Medical College, St. Louis, 1899; died in a hospital at West Palm Beach, April 14, aged 72, of myocarditis and angina pectoris.

Elizabeth Snyder, Los Angeles; Woman's Medical College of Pennsylvania, Philadelphia, 1885; member of the American Medical Association and the Medical Society of the State of Pennsylvania; died March 31, aged 87, of hypostatic pneumonia due to old myocardial insufficiency.

Paul E. Sundwall, Waukegan, Ill.; Chicago Medical School, 1925; member of the American Medical Association; on the staff of St. Therese's Hospital; died April 27, aged 57, of coronary thrombosis.

Alan Richard Welch, Lewistown, Ill.; St. Louis University School of Medicine, 1914; member of the American Medical Association; interned at the Kansas City General Hospital in Kansas City, Mo.; formerly on the staff of the Halstead Hospital, Halstead, Kan.; died March 31, aged 53, of myocardial infarction.

John Greenleaf White, Cerulean, Ky.; University of Nashville (Tenn.) Medical Department, 1894; Vanderbilt University School of Medicine, Nashville, 1894; member of the American Medical Association; served as president of the Bank of Cerulean before it closed; died in the Baptist Hospital, Memphis, Tenn., April 2, aged 74, of coronary thrombosis.

Henry Clay Woltmann, Jacksonville, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1903; member of the American Medical Association; vice president of the Morgan County Tuberculosis Association; secretary of the board of directors of the Morgan County Tuberculosis Sanatorium; on the staffs of the Passavant Memorial Hospital and Our Saviour's Hospital; served during World War I; vice president and director of the Jacksonville Savings and Loan Association; died April 18, aged 77, of acute dilatation of the heart.

DIED WHILE IN MILITARY SERVICE

Lyle Alva Condell ✠ Safford, Ariz.; University of Arkansas School of Medicine, Little Rock, 1935; diplomate of the National Board of Medical Examiners; interned at the San Bernardino County Charity Hospital in San Bernardino, Calif.; commissioned a lieutenant (jg) in the medical corps of the U. S. Naval Reserve on Oct. 21, 1941; promoted to lieutenant on June 15, 1942 and lieutenant commander on March 15, 1944; for twenty-eight months in combat service in the South Pacific; participated in five major engagements; attached to a destroyer; since returning to the United States had been stationed at Modesto, Alameda and Watsonville, Calif.; where he had been a naval flight surgeon and where he died April 22, aged 35.

Edward Joseph Humel Jr., Lakewood, Ohio; Western Reserve University School of Medicine, Cleveland, 1941; served an internship and residency at the University Hospitals in Cleveland; entered the medical corps, Army of the United States, as a first lieutenant, on Nov. 29, 1943; began active duty on July 8, 1944; died in Paris, France, April 1, aged 28, of poliomyelitis.

Thomas Maxwell Jr., Dayton, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1941; interned at the City of Detroit Receiving Hospital; entered the medical corps of the Army of the United States as a first lieutenant on July 25, 1942; began active duty Sept. 4, 1942; promoted to captain; completed a course in tropical medicine at the Army Medical School in 1943; had previously served with a bombardment group in the European theater; died in the Asiatic area Oct. 1, 1944, aged 31, of injuries received in an airplane accident.

Cornelia Ann Wyckoff, Southbury, Conn.; New York University College of Medicine, New York, 1941; interned at the Strong Memorial and Rochester Municipal Hospitals, Rochester, N. Y., and the Bellevue Hospital in New York; began active duty as a first lieutenant in the medical corps, Army of the United States, on March 3, 1944; had been stationed at Foster General Hospital in Jackson, Miss.; died in the Touro Infirmary, New Orleans, March 27, aged 28, of Clostridium welchi infection and heart disease.

Correspondence

IMMUNIZATION WITH MULTIPLE ANTIGENS

To the Editor:—In Queries and Minor Notes in THE JOURNAL, May 5, the question was asked concerning the effectiveness and possible disadvantages of immunization with multiple antigens. The mixture in question consisted of cholera vaccine, typhus vaccine and triple typhoid vaccine. The two answers submitted agreed as to its effectiveness but did not point out a serious disadvantage inherent in such a procedure. I refer to its use in the egg-sensitive individual.

At the Halloran General Hospital we have recently seen two Army nurses who gave a definite history of hypersensitiveness to eggs, on being questioned prior to inoculation with typhus vaccine. One gave a history of itching and swelling of the mouth and throat occurring after ingestion of one or two mouthfuls of soft boiled egg or of foods containing eggs. She could eat hard boiled eggs with impunity. The other gave a history of noting intensely itchy blotching of the skin of the face and neck after eating part of an egg.

Each was then intradermally tested with 1:100 and 1:10 dilutions of typhus vaccine.

The angioneurotic edema patient showed a large 3 plus reaction of immediate wheal-flare type, with pseudopodia but without production of constitutional symptoms. The vasomotor patient gave a negative intradermal reaction but showed, fifteen minutes later, an itchy blotching of the face, neck and back of such severity as to require subcutaneous injection of epinephrine 1:1,000 0.3 cc. for relief. Neither nurse was given typhus vaccine.

Now it is true that cases like these are not very common, but neither are they extremely rare. For this reason it is suggested that vaccines which contain egg protein should not be pooled with other vaccines for routine use. Also it is again emphasized that each patient be asked routinely as to the existence of egg protein hypersensitiveness prior to inoculation with vaccines containing egg protein, such as typhus, yellow fever, influenza and Rocky Mountain spotted fever.

A. H. RAYNOLDS, CAPTAIN, M. C., A. U. S.
Chief, Allergy Section.

FEMALE INFERTILITY

To the Editor:—The article on "Female Infertility" by Dr. George H. Gardner (THE JOURNAL, May 26) and the discussion which followed failed to give consideration to an important contributing factor to the high incidence of barren marriages today. This is the effect on fertility of several years of voluntary sterility.

A considerable percentage of the women who throng the offices of gynecologists today have prevented pregnancy in one way or another for two, three, five or more years following marriage. Many of these hapless women tell us that they have been influenced by the "planned pregnancy" ideas so well publicized in the past few decades. They were led to believe that the highly specialized reproductive function could be safely deferred until it was convenient to raise a family. Some say tearfully "my husband and I always intended to have children." They thought it wise to wait until business was better or the home they had planned was fully realized or, more recently, until the war was over.

Then, after postponing pregnancy for several years they decide that the opportune time has at long last arrived. But, all too frequently, when they discard their contraceptives or stop practicing "rhythm" they are chagrined and dismayed to find that the national bird of the Netherlands refuses to flutter anywhere near them.

On investigation we may find endometriosis, ovarian cysts, fibroids, endocervicitis or perhaps just the unexplainable lowered fertility that comes in either or both partners as the years roll by. It is not unreasonable to assume that many of these pathologic conditions have developed since marriage. Is it not likely that thousands of these now infertile women were able to bear children when they took their marriage vows?

It would seem to be an important duty of all who are interested in this problem to emphasize the ephemeral nature of fertility. Our young men and women should be urged to seize the golden opportunity of the first years of marriage and have their children while they are able to do so. We should tell them emphatically that if they deliberately thwart nature during this time they may permanently forfeit the inestimable privilege of parenthood.

ROY J. HEFFERNAN, M.D., Brookline, Mass.

THE GREEN COLOR OF A METHYLENE BLUE-BILIRUBIN MIXTURE

To the Editor:—Your editorial (THE JOURNAL, April 21) calling attention to the methylene blue test for bilirubin will be of value in that numerous papers or communications will soon appear denying the specificity of such a test. On theoretical grounds it was apparent that the green color which results when methylene blue is added to urine is merely related to the subtraction of colors from the visible spectrum by the substances involved in the test. No reaction takes place, because the test may be duplicated by merely holding a blue glass filter (Corning number 4303) in front of a test tube containing either yellow urine or a solution of bilirubin.

That this test is nonspecific and will be of little value may be seen from these spectroscopic observations and chemical procedures. Methylene blue appears blue because it has a strong absorption band in the red end of the spectrum (5,800-6,900 angstroms). This dye transmits most of the blue and practically all green light (4,200-5,800 angstroms). A trace of extreme red is also transmitted (6,900-7,000 angstroms), but for purposes of this discussion this small amount of red may be ignored. Bilirubin, dilute hemoglobin or any other yellow, orange or light red liquid absorbs strongly in the blue end of the spectrum (4,100-5,000 angstroms). The color of a solution or mixture depends on the wavelengths of light that are transmitted. In a mixture of methylene blue with any deep yellow or light red solution the methylene blue absorbs the red light, while the yellow test solution absorbs the blue. The green light is transmitted by both yellow and blue solutions, so the mixture appears green.

To investigate the nature and the specificity of this so-called test in a practical way, bilirubin was dissolved in alkaline water to give a red-yellow solution. This was examined through a spectroscope and found to absorb the blue light between 4,000 and 5,000 angstroms. A test tube containing this bilirubin solution was partially immersed in a beaker of dilute methylene blue in water which, when viewed through a spectroscope, was observed to absorb red light between 5,800 and 6,700 angstroms. In transmitted light the immersed portion of the tube appeared green. As expected, the spectroscope showed a green transmission band for the two superimposed, but unmixed, solutions extending from 5,000 to 5,800 angstroms. A mixture of the solutions transmitted the same band of green light. For final proof that the appearance of the green color in this proposed test is not related to any specific reaction, a green mixture of methylene blue and bilirubin was treated with sodium hydrosulfite. When the methylene blue was thus reduced to its leuko form the tube lost its green color and appeared to contain only the original red-yellow bilirubin solution.

Substances as diverse as commercial penicillin, riboflavin, porphyrins, hemoglobin and picric acid, when added to light

yellow urine or water, were found to give false positive tests for bilirubin. Since any deep yellow or light red solution exhibits this green color when mixed with methylene blue, there will probably be many more reports on the nonspecificity of this methylene blue test for bilirubin. (See also communication by Watson, Meads and Castle in THE JOURNAL, May 26, p. 308).

FRANK H. J. FIGGE, PH.D.
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THE TERM "WHOLE BLOOD"

To the Editor:—May I presume on your kindness to call to the attention of the members of the medical profession the difference between the term "whole blood" and "citrated blood," also called "modified blood."

The term whole blood is used incorrectly so often when citrated blood is meant that it seems to me that this error should be corrected.

Whole blood and citrated blood are as different as black and white. By far the most important life saving therapeutic agent we have today is properly matched whole blood, and it is my firm conviction that it is never going to be replaced by a substitute.

Citrated blood is a substitute for whole blood, and it should be used only in emergencies and when it is not practical to use whole blood. Severe reactions following the use of citrated blood are far more frequent than when whole blood is used.

Since we adopted the plan to determine the Rh factor on all recipients and give only Rh negative blood to Rh negative recipients, reactions have been eliminated when whole blood is used.

JOHN M. SCANNELL, M.D., Jamaica, N. Y.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, June 16, page 540.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, July 16-18. Part III. Various centers, June. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, June 27-29. San Francisco, Oct. 15-17. *Written.* Various centers, Oct. 15. Final date for filing application is Aug. 1. Candidates in the armed forces may take the examination at their station with the permission of their medical commanding officer. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison 5, Wis.

AMERICAN BOARD OF OPHTHALMOLOGY: Chicago, Oct. 4-6; and Los Angeles, January. Sec., Dr. S. Judd Beach, 56 Ivie Rd., Cape Cottage, Me.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I. Oral and Written.* New Orleans, Sept. 28-29, Philadelphia, Oct. 5-6, Chicago, Oct. 12-13 and San Francisco, Oct. 19-20. Final date for filing application is August 1. Sec., Dr. G. A. Caldwell, 3503 Prytania St., New Orleans 15.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Ia.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Oct. 19. *Oral.* New York, Dec. 7-8. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Fall, 1945. Final date for filing application is Aug. 1. Sec., Dr. B. R. Kirklin, Mayo Clinic, Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, October 24. Final date for filing application is Aug. 1. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: *Written.* Chicago, Dec. 9. *Oral.* Chicago, Feb. 19-22. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis 4.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Tearing of Esophageal Wall in Attempt to Remove Pork Bone.—The plaintiff swallowed a small pork bone, which became lodged in her esophagus. Within an hour thereafter, because of severe distress, she visited the defendant physician, a general practitioner, for treatment. According to the physician, he first examined her throat by using an illuminated tongue depressor but was unable to detect any foreign body. He then put on a head mirror and with an electric mirror in back and one in front of him and holding the patient's tongue with a sterile pad he thought he detected a foreign body in the throat. By means of a pair of laryngeal forceps about 10 inches long, with a piece of surgical cotton on the end, he proceeded to try to wipe this foreign body from the throat with a sweeping motion from below upward. He was unsuccessful in removing it and informed his patient that he could do nothing further and that the case was one for a specialist who could use an esophagoscope. He then called Dr. Carmody, a specialist, who instructed him to take roentgenograms and to send the patient to a hospital where the specialist could attend her. The defendant physician testified positively that he did not insert the forceps down the patient's esophagus and that it would have been physically impossible for his forceps to have reached the spot in the esophagus where Dr. Carmody testified he found the pork bone—namely, on the left side of the esophageal wall about opposite where the first rib makes a junction with the clavicle. The plaintiff and her husband, on the other hand, testified that the forceps the physician claimed he used and which were introduced in evidence were not the instrument used by the defendant. Their testimony seemed to indicate that the defendant wrapped some cotton around the end of a probe, which seemed about 14 inches long, longer than the forceps the defendant claimed he used, and that the defendant then put the instrument down the plaintiff's throat as far as he could. According to the plaintiff, the use of the probe "caused a sharp pain. Then the bone in my throat slipped. I didn't have that choking. Then he took the probe out and went over and wrapped it with cotton again" and then said if he was unsuccessful he would have to resort to a specialist. Prior to the defendant's operations, so the patient testified, there had been no hemorrhage but about the time she left his office to go to the hospital—approximately ten or fifteen minutes after the probing—some hemorrhage occurred. Dr. Carmody, the specialist, testified that later in the night in question by means of an esophagoscope he located and removed the pork bone. This operation involved placing the patient under an anesthetic and then inserting the instrument gradually down the esophagus. Basically, the instrument is a hollow tube within which run two wires; at the end of one of these is a small electric lamp with which the operator, by means of a reflector, can see the area just ahead of the esophagoscope; at the end of the other wire is a set of diminutive forceps with which the operator may take hold of objects. Dr. Carmody stated that he first located some cotton on the left side of the esophageal wall, about opposite where the first rib makes a junction with the clavicle, and that it was the cotton that led him to the foreign body. "I couldn't," he said, "see the foreign body. I saw the cotton. The cotton was on the foreign body. . . . The bone came out with it." Subsequent examination disclosed a tear in the esophageal wall and the bone or cotton, at the time of its removal, was inside, and not outside, the wall. No damage apparently was occasioned by the use of the esophagoscope itself. On account of the tear in the esophagus, the patient became ill; fluid developed in the pleural cavity; mixed infection—streptococcus empyema and also staphylococcus—occurred, and it was necessary to resort to liquid feeding for two weeks to prevent any solid food material working into the pleural cavity. Drainage of that cavity became imperative and the drainage tube remained in her side for approximately three months.

Subsequently the patient instituted an action for malpractice against the defendant physician, alleging apparently that the tear in the esophageal wall and her subsequent disability was occasioned by his negligence. At the trial, in addition to the testimony of the patient and her husband, the defendant physician, and Dr. Carmody, there was medical testimony that the piece of surgical cotton which was firmly adhering to the bone at the time of its removal by Dr. Carmody might have been swallowed by the plaintiff during the procedures instituted by the defendant and in its journey down the esophagus might have come into contact with the bone and adhered thereto. There was also medical testimony that the adherence of the cotton to the bone was so firm that the impact between the bone and the cotton must have been with more force than that involved in the act of swallowing. Although the defendant physician had testified that the plaintiff complained of the foreign object being in the upper reaches of the throat, Dr. Carmody testified that when the defendant physician telephoned him he stated that he had a patient in his office who had a bone in her esophagus. Several medical witnesses, called by the patient, in answer to hypothetical questions, testified that, assuming the existence of a bone in the esophagus and a probing for it in a manner related by the patient, such a procedure was not good medical practice under present standards in the profession for a general practitioner and would be dangerous to the patient. The defendant's evidence went to the point of showing that he did not insert any instrument in the patient's esophagus; that the forceps he used did not and could not reach beyond the cricoid constrictor located at the entrance to the esophagus, while the plaintiff's evidence went to the point that without preliminary examination, either by way of x-ray or esophagoscope, the defendant physician introduced a probe into the patient's esophagus causing the injury described. After a series of motions the court submitted the case to a jury, which returned a verdict in favor of the patient and judgment was entered thereon. The defendant physician appealed to the Supreme Court of Colorado.

The defendant physician at appropriate times during the trial moved for a nonsuit, directed verdict and for a new trial, all of which motions were denied. These motions, said the Supreme Court, involved the one question as to whether or not there was sufficient competent evidence to warrant the submission of the case to the jury. We believe that there was and the trial court's denial of the motions was proper.

The following instruction was given by the trial court to the jury:

> You are instructed that in judging the proper degree of skill to be exercised by a physician or surgeon in any given case, regard is to be had to the advanced state of the profession at that time, and that a physician or surgeon by holding himself out to the world as such impliedly contracts that he possesses the reasonable degree of skill, learning and experience which good physicians and surgeons of ordinary ability and skill, practicing in similar localities, ordinarily possess, and that he will use his skill with ordinary care and diligence according to the circumstances of the case, and if you find that the defendant in this case did not use ordinary care and diligence then you will find for the plaintiff.

The defendant contended that this instruction was improper because it failed to state that the defendant, as a general practitioner, was not expected to have or to exercise the skill of a specialist in treating cases of the kind involved here. This instruction, answered the court, is a proper one as relating to a physician in general practice. The standard to which he is held is ordinary ability and skill to be applied with ordinary care and diligence according to the circumstances of the case. There is nothing in the language of the instruction complained of suggestive of a specialist.

The physician complained of the instruction just quoted on the additional ground that it contained no statement that to justify a finding for the patient there must, in addition to a finding of lack of ordinary care and diligence on the part of the physician, also be a finding that such lack of ordinary care and diligence was the proximate cause of the injuries complained of. This instruction, said the court, was proper when read in connection with all the other instructions, including one instruction which is a standard instruction relating to the burden of proof and still another instruction which stated that a physician "does not warrant success and is not responsible for want of success unless that want results from failure to exercise that reasonable care, diligence and skill" previously referred to in instructions tendered the jury.

The court accordingly affirmed the judgment in favor of the patient.—*Dixon v. Norberg, 157 P. (2d) 131 (Colo., 1945).*

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the Federal Security Agency

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act, and in cases in which they refer to drugs and devices they are designated D.D.N.J. and foods, F.N.J. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the type of nostrum; (6) the reason for the charge of misbranding, and (7) the date of issuance of the Notice of Judgment.]

Allan's Red Wash Combination.—Allan & Co., Inc., St. Louis, and John G. Ayars. Shipped between Sept. 18 and Oct. 1, 1941. Consisted of a bottle of "Red Wash" and one of "Sa-Ura Emulsion." The "Wash" was essentially small amounts of cresol, boric acid, glycerin, water and compounds of aluminum, ammonium and zinc sulfates. The "Sa-Ura Emulsion" contained chiefly castor oil and volatile oils, including sandalwood, turpentine and balsam of copaiba. Both products misbranded because falsely represented as effective in curing, mitigating, treating or preventing social diseases.—[*D. D. N. J., F. D. C. 855; May 1944.*]

Be Plex Vitamin B Complex with Minerals and Iron.—Hale Drug Company, Birmingham, Ala. Shipped Jan. 9, 1942. Composition: product contained not more than 25 per cent of the 669 International units of vitamin B_1 per fluid ounce declared on label. Adulterated for this reason. Misbranded because of false and misleading label representations that in cases of vitamin deficiency product would be valuable as an aid to promote appetite and a protection to the body against "nerve disorder," and a help in certain cases of retarded growth, constipation, migraine, headaches and some other things, whereas it would not be efficacious for such purposes.—[*D. D. N. J., F. D. C. 878; May 1944.*]

Crab Orchard Concentrated Mineral Water.—Crab Orchard Mineral Water & Crystal Company, Inc., Crab Orchard, Ky. Shipped March 23, 1940. Composition: dissolved mineral matter, chiefly magnesium and sodium sulfates, with smaller amounts of other salts. Misbranded because labeling falsely represented that the water would be an effective treatment and alleviation of conditions usually calling for a sojourn at a mineral spring; that it would relieve inveterate chronic diseases, cleanse the system of toxins and waste matter, and remove the dangers of constipation; that it would benefit conditions arising from disordered liver and kidneys, prevent attacks on the blood corpuscles by toxins engendered in the system from defective filtration or cleansing; that it would prevent depletion of the nerve cells, safeguard beauty in women and keep men fit; that it would be beneficial in treating constipation, rheumatism, headaches, influenza, colds and some other disorders, keep the blood stream pure, help skin blemishes and eruptions, maintain a clean system, improve the appetite and enable one to sleep and feel better.—[*D. D. N. J., F. D. C. 889; May 1944.*]

Glendage.—Joseph A. Piuma, Los Angeles. Shipped August 1, 1941. Composition: tablets, each containing glandular material, including ⅛ grain of thyroid, with nux vomica extract (containing strychnine), a phosphide such as zinc phosphide, and a laxative drug, such as cascara sagrada extract. Misbranded because of false representation of glandular substance present, since such substances were not physiologically or therapeutically active when taken by mouth as directed.—[*D. D. N. J., F. D. C. 890; May 1944.*]

McBrady's Hair Pomade.—Bernard McBrady, trading as J. E. McBrady & Company, Chicago. Shipped July 28 and 29 and Dec. 12, 1941. Composition: essentially a small amount of a fatty acid such as stearic acid, incorporated in a base of petrolatum and wax. Misbranded because label falsely represented that product was an effective cure or preventive of stubborn and falling hair, would give the hair a better chance to grow, cause it to grow faster, and soften and limber it.—[*D. D. N. J., F. D. C. 887; May 1944.*]

Real's Antiseptic Medicated Skin Cream.—Baker Drug Corporation, Norfolk, Va. Shipped Feb. 12 and March 21, 1942, the earlier shipment being made in the name of Joseph Friedberg. Composition: essentially small amounts of potassium hydroxide, volatile oils, including menthol, eucalyptol and oil of bergamot, and a trace of phenol in a base of stearic acid, petrolatum and beeswax. Bacteriologic examination showed article devoid of antiseptic properties. Adulterated because strength and quality fell below represented antiseptic standard, and misbranded for the same reason.—[*D. D. N. J., F. D. C. 864; May 1944.*]

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Anesthesiology, New York

6:113-224 (March) 1945

Recent Developments in Respiratory Physiology Related to Anesthesia. C. F. Schmidt.—p. 113.
Clinical Observations on Use of Curare in Anesthesia. R. J. Whitacre and A. J. Fisher.—p. 124.
Blast Injuries and Their Anesthetic Management. S. J. Martin and J. M. Schwab.—p. 131.
Action of Morphine in Slowing Heart Rate of Unconditioned Dogs. C. R. Allen, Q. Murphy and W. J. Meek.—p. 149.
Spinal Anesthesia for Cesarean Section. A. M. Torrie.—p. 154.
Anesthesia: XVII. Cardiac Effects and Blood Gases under Anesthesia with Propethylene. W. E. Evans Jr. and J. C. Krantz Jr.—p. 159.
Effect of Varying Moisture Content of Soda Lime on Efficiency of Carbon Dioxide Absorption. J. Adriani.—p. 163.
Experiences with Anesthesia in an Army Hospital in New Guinea. L. J. Hampton and H. H. Hammett Jr.—p. 173.
Selection of Anesthesia for Physiologic Experiments: Use of Oxford Ether Vaporizer. A. D. Foster Jr., C. Neumann and E. A. Rovenstine.—p. 181.
Apparatus for Administering Pentothal Sodium. R. C. Adams.—p. 191.

Journal of Clinical Endocrinology, Springfield, Ill.

5:61-118 (Feb.) 1945

*Cushing's Syndrome Without Adenomatous or Hyperplastic Changes in Pituitary Body or Adrenal Cortices and Complicated by Alkalosis: Report of Case with Necropsy. H. E. Cluxton Jr., W. A. Bennett, M. H. Power and E. J. Kepler.—p. 61.
Relationship of "Crooke's Changes" in Basophilic Cells of Anterior Pituitary Body to Cushing's Syndrome (Pituitary Basophilism). E. J. Kepler.—p. 70.
Studies on Renal Excretion of Water and Electrolytes in Cases of Addison's Disease. J. Reforzo-Membrives, M. H. Power and E. J. Kepler.—p. 76.
Hypoparathyroidism of Probable Encephalopathic Origin. N. J. Winer.—p. 86.
*Review of 100 Cases of "Diabetic Neuropathy" Followed from One to Ten Years. A. Rudy and S. H. Epstein.—p. 92.
Relationship of Normal and Hyperactive Ovary to Menstruation and Endometrial Hyperplasia. C. G. Hartman.—p. 99.

Cushing's Syndrome.—Cluxton and his associates report the clinical history and necropsy of a woman, aged 27, who came to the Mayo Clinic presenting most of the features of Cushing's disease. The absence of adenomas, neoplastic or hyperplastic changes in the pituitary body, thymus or adrenal cortices and the associated alkalosis that was present during the life of the patient are elements of additional interest. The patient's illness could not be attributed to any demonstrable anatomic abnormality if one excepts the hyaline changes that were found in the basophilic cells of the anterior lobe of the pituitary body. The physiologic significance of these changes is not known, but one of the authors believes that these changes are secondary or retrograde rather than an alteration of fundamental significance in the causation of the syndrome and that the clinical manifestations of the patient's illness were an expression of an abnormal adrenal cortical function of a hypersecretory character in spite of the fact that there was no histologic evidence to support this view. This case also presents one more instance of alkalosis and low potassium occurring in Cushing's syndrome, 3 cases having been previously reported from the Mayo Clinic. In some cases alkalosis occurs solely as the result of abnormal adrenal cortical function.

Diabetic Neuropathy.—Rudy and Epstein review 100 cases of diabetic neuropathy followed from one to ten years. The incidence according to clinical localization was neuritis 54, myelopathy 26, encephalopathy 4, encephalomyelopathy 5 and neurogenic bladder disturbances 11. Diabetic neuropathy is a generalized neurologic disturbance. It is observed not only in the acute stage of diabetes but also soon after the control of the glycosuria and hyperglycemia and in the chronic and even mild cases of diabetes. This neuropathy develops most frequently in patients over 50 years of age and is preceded or accompanied by considerable loss of weight. Symptoms and signs of a vitamin B complex deficiency are frequently associated with it. The vitamin deficiency is secondary, and it appears to be caused by the disturbed metabolism and at times by an associated chronic infection or other complication. A demonstrable dietary insufficiency is a factor only in certain cases. Complete recovery from the neuropathy is uncertain and slow, but it occurs following prolonged therapy with vitamin B and control of the glycosuria and hyperglycemia.

Journal of Experimental Medicine, New York

81:315-404 (April) 1945

Studies on Flexner Group of Dysentery Bacilli: I. Specific Antigens of Shigella Paradysenteriae (Flexner). W. F. Goebel, F. Binkley and E. Perlman.—p. 315.
Id.: II. Chemical Degradation of Specific Antigen of Type Z Shigella Paradysenteriae (Flexner). F. Binkley, W. F. Goebel and E. Perlman.—p. 331.
Id.: III. Antibody Response in Man Following Administration of Specific Antigen of Type V Shigella Paradysenteriae (Flexner). E. Perlman, F. Binkley and W. F. Goebel.—p. 349.
Nutrition of Host and Natural Resistance to Infection: I. Effect of Diet on Response of Several Genotypes of Mus Musculus to Salmonella Enteritidis Infection. H. A. Schneider and L. T. Webster.—p. 359.
New Virus Disease of Pigeons: I. Recovery of Virus. J. E. Smadel, E. B. Jackson and J. W. Harman.—p. 385.
Cirrhosis of Liver in "Donor" Dogs Fed High Fat Diet and Subjected to Repeated Bleedings. R. L. Holman.—p. 399.

Journal National Malaria Society, Tallahassee, Fla.

4:1-76 (March) 1945. **Partial Index**

Entomologic Problems in Malaria Control. G. H. Bradley.—p. 1.
*Suppressive Treatment of Malaria in Military Forces. O. R. McCoy.—p. 9.
Inhibitory Effect of Pyridoxine on Activity of Quinine and Atabrine Against Avian Malaria. A. O. Seeler.—p. 13.
Relation of Plants to Malaria Control on Impounded Waters, with Suggested Classification. A. D. Hess and T. F. Hall.—p. 20.
*Importation of Exotic Anophelines into United States. J. A. Mulrennan.—p. 56.
Recent Advances in Epidemiology of Malaria. R. B. Watson, H. W. Brown and D. S. Ruhe.—p. 58.
Statement of Progress, Kentucky Reservoir Malaria Control Program. F. E. Gartrell.—p. 63.
Malaria Mortality and Morbidity in United States for Year 1943. E. C. Faust, J. A. Scott and G. E. McDaniel.—p. 66.

Treatment of Malaria.—According to McCoy, atabrine has proved much more effective than quinine for suppression of malaria and, in general, is better tolerated and preferred by troops. A most important experience gained is the demonstration of the effectiveness of atabrine in preventing the development of falciparum malaria. When atabrine is taken in doses of 0.6 or 0.7 Gm. per week during and for several weeks following exposure to falciparum infection, appearance of symptoms is consistently prevented not only during suppressive treatment but also after medication is discontinued. Suppressive doses of atabrine apparently act as curative doses in this type of malaria. In this respect atabrine is far superior to quinine. As a result of the extensive use of atabrine for suppressive treatment, falciparum malaria has been much less of a problem in the military forces than was anticipated at the start of the war. Vivax malaria, on the other hand, is suppressed but not cured by atabrine. Relapses of vivax malaria experienced after the cessation of suppressive medication constitute a major portion of the Army's malaria problem. In units heavily seeded with vivax malaria it may be necessary to continue suppressive treatment in order to maintain military effectiveness even though no further exposure to infection occurs.

Importation of Exotic Anophelines.—According to Mulrennan and his associates the present emergency has greatly increased the possibility of exotic species of insects gaining ingress and becoming established in North America. This can be partially demonstrated by the fact that alien anophelines have been collected in two localities in Florida, with the infer-

ence on aircraft importation, since the specimens were collected adjacent to air fields. Emphasis is placed on the insecticiding of aircraft at the port of debarkation and a second application and inspection at the port of entry.

Journal of Nervous and Mental Disease, New York

101:205-310 (March) 1945

Healing Mechanisms in Shock Treated Neurotic Patient. J. D. Moriarty and A. A. Weil.—p. 205.
War Strains and Mental Health. A. B. Stokes.—p. 215.
Syphilitic Hepatitis and General Paresis Occurring Simultaneously: Report of Case. R. F. Gayle Jr. and W. B. Quisenberry.—p. 220.
Psychiatry and Propaganda. W. Eliasberg.—p. 225.
Observation on Interrelationship of Group and Individual Psychotherapy. J. W. Klapman.—p. 242.
Shock Treatment in Psychopathic Personality. H. F. Darling.—p. 247.
Fatigue as Precipitating Factor in Latent Epilepsy. M. H. Weinberg.—p. 251.
Problems of Orphanhood. S. Schryver.—p. 257.
Work of Chaplain in State Hospital for Mental Disorders. A. W. Scully.—p. 264.
New Approach to Problem of Hysteria. F. Pollak.—p. 268.
Frost Bites and Effects on Human Body. H. K. Craig.—p. 272.

101:311-400 (April) 1945

Electroencephalographic and Neurologic Studies of Homosexuals. D. Silverman and W. R. Rosanoff.—p. 311.
Persistence of Symptoms in Psychoneurotic Ex-Soldier. D. Pratt.—p. 322.
Cerebrospinal Fluid After Electric Convulsive Therapy. J. F. Maddux and C. K. Aldrich, with technical assistance of J. J. Blair.—p. 330.
Insulin, Cardiazol and Electroshock Treatment in Palestine During the Last Five Years. K. Blumenthal.—p. 332.
Psychiatric Factors Influencing Learning. G. N. Thompson.—p. 347.
Different Forms of Diffuse Sclerotic Process—Pelizaeus-Merzbacher Disease, Struempell's Familial Spastic Spinal Paralysis, Leukodystrophy—in One Family. M. Kastan.—p. 357.
*Hemiballismus: Clinicopathologic Study of 2 Cases. H. Kelman.—p. 363.
*Intraspinal Thiamine Chloride in Treatment of Gastric Crisis or Lightning Pains in Tabes Dorsalis: Report of 8 Cases. B. H. Kesert and M. O. Grossman.—p. 372.
Patient's Reaction to "Lunacy" Charge. L. Kerschbaumer.—p. 378.

Hemiballismus.—According to Kelman, hemiballismus is a syndrome characterized by violent uncontrollable, purposeless, throwing (ballistic) movements of one upper extremity or of the entire half of the body. The lesions in the corpus luysi are mainly due to hemorrhages, softenings or emboli, but they may also be due to infections, toxins and degenerative conditions. The author presents the clinical and pathologic aspects of 2 cases of hemiballismus. The first patient, a man aged 66, died within three months of the first attack. The episodic nature of the attacks suggests that they were due to an irritative process within the corpus luysi. In this case a destructive lesion was found. The destructive process is evidence of the previous existence of a dysphysiologic state. Such transitory states might occur and lead to attacks of hemiballismus without leaving significant evidence in the form of cellular changes in the corpus luysi or of degeneration in its afferent or efferent tracts. The nature of the attacks, at times involving only the hand, at others including also the face, finally to affect the lower extremity, confirm clinically that somatotopic localization exists in the corpus luysi. The second patient, a man aged 56, lived eight months after the onset of the abnormal movements. It has been stated that volition and psychic factors do not affect the movements. When this man was at rest the movements were least. When he made attempts to use his extremities spontaneously or on command as well as when he became emotionally disturbed, the movements became exaggerated. Neither of the 2 patients could voluntarily control the movements. In the second patient a metastatic nodule invaded and destroyed the tip of the oral pole of the corpus luysi. At necropsy the major lesion was so placed as to affect essentially the subthalamicotegmental fibers. This seems to indicate that a lesion limited to afferent tracts might cause hemiballismus. It also tends to prove the passage of most of the fibers contralaterally but also indicates that some pass homolaterally. The major movements were on the right side, but some were also present on the left.

Intraspinal Thiamine Hydrochloride in Tabes Dorsalis.—Kesert and Grossman say that in 1942 Stone reported good results from the use of intraspinal and oral vitamin B in cases of tabes dorsalis. Not only were the shooting pains in tabes relieved, but improvement in gait, bladder control and muscular tone was noted. The authors proceeded to try this form of therapy in all of their cases of tabes dorsalis, mainly for relief of shooting pains and gastric crisis. Up to the present, 8 patients have been followed. They were given from one to six intraspinal injections in doses ranging from 50 to 100 mg. The pains were intensified for a period of twelve hours after the injection, but then relief followed, which was partial or complete and lasted from several weeks to months, sometimes longer. Some of the patients were receiving thiamine hydrochloride orally or subcutaneously, but immediate relief of the intractable pains was due to the action of the thiamine hydrochloride given intraspinally. The use of narcotics and chordotomy can be avoided when thiamine hydrochloride is injected for tabetic and gastric crises.

Journal of Neurophysiology, Springfield, Ill.

8:77-134 (March) 1945

Electric Excitability of Nerve-Muscle Fiber Preparations. S. W. Kuffler.—p. 77.
Choreiform Movements in Dog Suffering from Corticostriatal Disease. Hsiang-Tung Chang.—p. 89.
Electroencephalogram of Different Cortical Regions of Normal and Anesthetized Cats. S. L. Clark and J. W. Ward.—p. 99.
Action of Veratrine on Nerve-Muscle Preparations. S. W. Kuffler.—p. 113.
Projection of Retina on Superior Colliculus of Cats. Julia T. Apter.—p. 123.

Journal of Nutrition, Philadelphia

29:155-222 (March) 1945

*Effects of Variations in Dietary Vitamin C on Physical Well Being of Manual Workers. R. E. Johnson, R. C. Darling, F. Sargent and P. Robinson with the technical assistance of M. Bartlett and A. Kibler.—p. 155.
Effect of Chain Length of Dietary Fatty Acid on Fatty Liver of Choline Deficiency. D. Stetten Jr. and J. Salcedo Jr.—p. 167.
Fatal Myocarditis in Choline Deficient Rats Fed Ethyl Laurate. H. D. Kesten, J. Salcedo Jr. and D. Stetten Jr.—p. 171.
Observations on Riboflavin Excretion by Adult Male. Dorothy R. Hagedorn, Emma D. Kyhos, O. A. Germek and E. L. Sevringhaus.—p. 179.
Niacin (Nicotinic Acid), Essential Growth Factor for Rabbits Fed Purified Diet. J. G. Wooley and W. H. Sebrell.—p. 191.
Effect of Sunshine on Ascorbic Acid and Riboflavin Content of Milk. A. D. Holmes and C. P. Jones.—p. 201.
Citrate Metabolism of Preschool Children. Esther R. Metcalf and Milicent L. Hathaway.—p. 211.
Further Studies on Cystine, Methionine and Choline in Chick Diets. H. J. Almquist and C. R. Grau.—p. 219.

Dietary Vitamin C and Physical Well Being of Manual Workers.—Johnson and his associates report experiments conducted during the summer in Civilian Public Service Camp 32, Campton, N. H. The 24 volunteer subjects were engaged in a variety of jobs associated with the work schedule of the camp, which included clerical work, kitchen work, camp maintenance, farming, clearing trails and road building. The range of daily caloric expenditures, depending on the subject's job, was estimated to be 2,400 to 5,000. There were four groups of subjects. The "deficient group" was to demonstrate the effects of total deficiency, the "supplemented deficient group" the effects of 75 mg. of ascorbic acid daily, the "normal control group" the effects of a good normal diet and the "supplemented normal control group" the effects of a normal diet supplemented with 75 mg. of ascorbic acid daily. If the previous diet has been good, total deprivation of vitamin C for two months does not lead in manual workers to detectable deterioration in physical vigor, to inefficiency in the day's work or to unpleasant symptoms, provided the daily diet is adequate in all nutrients other than vitamin C. Such deprivation may occasionally lead to minimal changes in the gums and does produce severe desaturation as measured by serum and urinary levels of vitamin C and by tolerance tests. When given in doses of 25 mg. three times daily, 75 mg. of ascorbic acid a day appears adequate to maintain or even to increase the body stores of the vitamin in a majority of men held for two months on a diet totally deficient in ascorbic acid. Supplements of 75 mg. of ascorbic acid a day when added to a good normal diet are of no detectable benefit to manual workers over a period of two months with respect

to general well being, physical vigor for hard work and efficiency in the day's work. Such supplements do lead to increased stores of vitamin C, as evidenced by serum and urinary levels and by tolerance tests.

Journal of Pediatrics, St. Louis

26:209-312 (March) 1945. **Partial Index**

Rheumatic Fever and the American Academy of Pediatrics: General Purpose and Scope. A. T. Martin.—p. 209.
*Salicylate Therapy in Acute Rheumatic Fever. R. Wégria and Katharine Smull.—p. 211.
Acute Salicylate Poisoning. A. F. Hartmann.—p. 214.
Sulfonamide Prophylaxis for Prevention of Rheumatic Recurrences. Ann G. Kuttner.—p. 216.
Rheumatic Heart Disease and Physical Fitness of Nation as Seen by Selective Service. L. G. Rowntree.—p. 220.
Plan for Rehabilitation for Rheumatic Subjects. J. G. F. Hiss.—p. 230.
Mobilization Against Rheumatic Fever. G. M. Wheatley.—p. 237.
General Statement Regarding State Rheumatic Fever Programs. Betty Huse.—p. 245.
Rheumatic Fever and American Academy of Pediatrics: Public Health Aspects; Epidemiology. T. D. Jones and B. E. Massell.—p. 262.
Indications for and Limitations of Treatment of Poliomyelitis. J. A. Key.—p. 265.
Paroxysmal Tachycardia in an Infant the Fourth Day of Life: Recovery with Digitalis. P. J. Howard.—p. 273.
Asphyxia Neonatorum: An Evaluation—Etiology and Treatment. H. R. Litchfield.—p. 279.
Penicillin Therapy of Pneumococcic Meningitis: Report of Case with Recovery Following Intraspinal, Intracisternal and Intraventricular Administration of Penicillin. Katharine H. Baird.—p. 287.
Correlation of Symptomatology with Enterozoic Parasitism in Children. R. L. Brown.—p. 291.
*Blood Plasma in Treatment of Encephalitis Lethargica and Polioencephalitis: Preliminary Report. P. Nicholson.—p. 298.

Salicylate Therapy in Acute Rheumatic Fever.—Wégria and Smull compared the course of acute rheumatic fever in two groups of patients, one "adequately" treated according to Coburn's standards and one with smaller doses. In the adequately treated group the serum salicylate levels ranged between 350 and 500 micrograms. The other group received such doses of salicylate that serum levels in most patients were constantly below 250 micrograms per cubic centimeter and in a few patients reached "optimal" levels only for short periods. The course of the disease was not shorter in the adequately treated group.

Blood Plasma in Treatment of Encephalitis.—Nicholson reports a case of lethargic encephalitis and a case of polioencephalitis in both of which pooled adult plasma was given intravenously with favorable results. He suggests that this method of treatment might be used in epidemics of poliomyelitis, because the case presented here was one of a severe encephalitic type and gave the use of blood plasma a severe test.

Journal of Urology, Baltimore

53:427-506 (March) 1945

Preventive Treatment of Calcium Urolithiasis: Important Role of Early and Frequent Roentgenographic Examinations. R. H. Flocks.—p. 427.
Urolithiasis in Soldier. A. H. Milbert and I. Gersh.—p. 440.
Relationship of Epithelial Buds to Carcinoma of Pelvis of Kidney, Ureter and Bladder. A. E. Bothe.—p. 451.
Endometriosis of Bladder. H. L. Kretschmer.—p. 459.
End Results of Prostatectomy: Five Year Survey. Lowrain E. McCrea.—p. 466.
Simplified Suprapubic Prostatectomy. D. K. Rose.—p. 470.
Transurethral Resection for Men 80 or More Years of Age. C. W. Latchem and J. L. Emmett.—p. 482.
New Suprapubic Drainage Apparatus for Use with Suction. R. L. Smith.—p. 486.
Role of Urologist in Military Service. G. J. Thompson.—p. 491.
Studies Concerning Renotropic Action of Pituitary Extracts. H. Selye and Charlotte Hollett.—p. 498.
Chancroid Disease in Female. G. G. Allison.—p. 503.

Kentucky Medical Journal, Bowling Green

43:61-94 (March) 1945

Surgical Aspects of Chronic Dyspepsia. I. Abell.—p. 70.
Medical Aspects of Tropical Diseases. A. McMahon.—p. 76.
Nutrition: Its Relation to Deficiency Diseases. J. B. Youmans.—p. 83.

43:95-118 (April) 1945

Chemotherapy (Penicillin). D. G. Anderson.—p. 99.
Concerning Commencement of Things Medical. W. D. MacNider.—p. 103.
Ablatio Placentae. J. L. Keyes.—p. 106.
Historical Notes on Penicillium Notatum. H. P. Morgan.—p. 109.
Poliomyelitis. J. A. Toomey.—p. 111.

Medical Annals of District of Columbia, Washington

14:141-192 (April) 1945

Psychiatrist Looks at Constitution and Environment and Is Puzzled. B. Karpman.—p. 141.
*Treatment of Gonococcal Vaginitis in Children with Penicillin. L. K. Sweet and L. E. Putnam.—p. 148.
Allergic Nose. H. H. Diamond.—p. 151.
Unusual Case of Dissecting Aneurysm of Aorta. S. A. Steiner.—p. 155.

Penicillin for Gonococcic Vaginitis of Children.—Sweet and Putnam used the sodium salt of penicillin in the treatment of 15 children with gonococcic vaginitis, 1 with vaginitis and conjunctivitis and 1 with conjunctivitis. The diagnosis in 16 cases was established by culture. The penicillin was given in multiple injections over a period of from twelve to twenty-seven hours. The exact schedule of dosage remains to be determined, but the authors think that children of 7 years or under probably will respond to a dose of 50,000 units given over twelve hours, while older patients should be given approximately 100,000 units of penicillin. A single large dose of regular sodium penicillin is not effective, although it is possible that two or three injections of 25,000 to 50,000 units each at intervals of two or three hours may be curative. This regimen will be investigated, since, if satisfactory, it would greatly simplify the office or clinic treatment of such patients.

Public Health Reports, Washington, D. C.

60:317-344 (March 23) 1945

Comparison of Effect of Penicillin and Immune Serum in Treatment of Experimental Leptospirosis in Young White Mice and in Hamsters. C. L. Larson and J. J. Griffitts.—p. 317.
*Penicillin Treatment of Leprosy: Clinical Note. G. H. Faget and R. C. Pogge.—p. 324.

60:345-372 (March 30) 1945

Titration of Clostridium Perfringens (Welchi) Antitoxin by Its Antihemolytic Activity. Sarah E. Stewart.—p. 345.
Preliminary Report on Identification of 2,2 Bis (p-Chlorophenyl)-1,1,1 Trichlorethane (DDT) in Excreta of Poisoned Rabbits. E. F. Stohlman.—p. 350.
Psittacosis: Occurrence in United States and Report of 97 per cent Mortality in Shipment of Psittacine Birds While Under Quarantine. G. L. Dunnahoo and B. C. Hampton.—p. 354.

60:373-400 (April 6) 1945

Experimental Chemotherapy of Burns and Shock: VIII. I. Effects of Potassium Administration, of Sodium Loss, and Fluid Loss in Tourniquet Shock. H. Tabor and S. M. Rosenthal.—p. 373.
Nuisance Complaints and Municipal Health Department Practices. M. A. Pond.—p. 381.

60:401-428 (April 13) 1945

Experimental Chemotherapy of Burns and Shock: VIII. II. Electrolyte Changes in Tourniquet Shock. H. Tabor and S. M. Rosenthal.—p. 401.

Penicillin in Leprosy.—According to Faget and Pogge, penicillin was tried at the National Leprosarium in the treatment of 7 cases of leprosy in doses of 50,000 to 100,000 units daily, which were continued in some cases for a month's time. No specific beneficial effect could be attributed to this treatment. Subsequently two of the previously treated patients and 2 new patients were given much larger doses of penicillin without effect.

Union Médicale du Canada, Montreal

74:421-570 (April) 1945

Pericoronary Neurectomy Associated with Ligature of Great Coronary Vein in Treatment of Some Forms of Coronary Disease. M. Fauteux.—p. 424.
Cutaneous Allergy. A. Marin.—p. 432.
*Roentgenotherapy in Treatment of Inflammatory Lesions. O. Dufresne.—p. 439.
Bronchoscopy at Bed of Patient. V. Latraverse.—p. 448.
Atypical Case of Miliary Tuberculosis. Y. Laurier.—p. 452.
Hypertrophic Stenosis of Pylorus. A. Pettigrew.—p. 458.
Hypertrophic Stenosis of Pylorus in the Newborn. J. C. Côté.—p. 461.

Roentgenotherapy in Inflammatory Lesions.—Dufresne says that experimental studies justify the conclusion that x-rays in small doses activate the proliferation of lymphoid tissues, augment the mobilization of lymphocytes, increase the bacteriolytic power of the blood and improve the local defense. His clinical experiences with x-rays cover a period of fifteen years. The majority of acute infections in which Dufresne has employed roentgenotherapy have been superficial, such as ery-

sipelas, furunculosis, anthrax, sycosis and herpes zoster. The only cases of deep acute infections in which irradiation was used were pelviperitoneal ones associated with cancer of the uterus. The number of subacute and chronic infections treated with x-rays has been comparatively larger than that of acute infections; they include among others acne, mycosis fungoides, cholecystitis, rectitis, adenitis, tuberculous adnexitis and epididymitis, poliomyelitis, myositis and osteoarthritis. In acute infections two or three small doses of from 25 to 75 roentgens each are usually sufficient to abort the attack. In subacute infection six to eight doses of from 100 to 125 roentgens each are administered at intervals of two or three days. In chronic infections irradiations extend over a long period and may reach a total of from 2,000 to 2,500 roentgens. The more superficial the infection, the lower should be the voltage and the lighter the filtration; the deeper the infection, the higher should be the voltage and the stronger the filtration.

War Medicine, Chicago

7:71-142 (Feb.) 1945

*Tsutsugamushi Fever: Clinical Observation in 195 Cases. M. G. Berry; A. S. Johnson Jr., and S. E. Warshauer.—p. 71.
*Cardiac Complications of Tsutsugamushi Fever (Scrub Typhus): Investigation of Their Persistence. H. D. Levine.—p. 76.
Experimental Human Burns: Partial Report. W. F. Ashe Jr. and L. B. Roberts.—p. 82.
Interservice Consultations in One Army General Hospital: Comments, with Particular Reference to Section on Gastroenterology. S. Morrison.—p. 84.
*Typhoid in Previously Immunized Subjects: Report of 7 Cases, with Discussion of Diagnosis, Clinical Course and Complications. J. L. Tullis.—p. 95.
Sensitivity of Bacteria from Infected Wounds to Penicillin: II. Results in 112 Cases. E. Gallardo.—p. 100.
Hemoglobinuria: Report of 10 Cases of Its Occurrence in Negroes During Convalescence from Malaria. H. E. Swantz and M. Bayliss.—p. 104.
Paracolon Bacilli: Study of Fifty-Three Isolated Strains, with Note on Pathogenicity. M. Michael Jr. and V. T. Harris.—p. 108.

Tsutsugamushi Fever.—Berry and his associates present the clinical aspects of tsutsugamushi fever among 195 patients admitted to two station hospitals in New Guinea between December 1942 and June 1944. Eighty-five of these patients were admitted directly to the hospitals early in the course of their illness; the remainder were transferred from other hospitals for convalescent management. They stress that tsutsugamushi fever is an acute infectious systemic disease in which the most striking features are pronounced toxemia and widespread damage to the capillaries and arterioles. The physician may be inclined to attribute low blood pressure, cyanosis and tachycardia to myocardial failure when in fact they are due to peripheral vascular collapse. The clinical picture is more analogous to shock than to heart failure. Clinically there is no severe irreversible damage to the myocardium. The asthenia and tachycardia which occur in convalescence are no more pronounced than those which may be expected to follow any prolonged severe illness. One must carefully avoid giving the patient the impression that he has heart disease, because in patients with psychoneurotic tendencies a "cardiac neurosis" may result, and when this occurs it is extremely difficult to return the patient to duty. Although the pathognomonic pulmonary lesion is vascular, atelectasis is of clinical importance and occurs more frequently than has been recognized and apparently is secondary to the pneumonitis and bronchiolitis that are part of the disease. The rapid shallow respiration which one sees in severely ill patients is of pulmonary rather than cardiac origin. The pathologic changes found in the brain and leptomeninges, like the myocardial changes, are reversible, and if the patient survives his illness permanent sequelae are not to be expected.

Cardiac Complications of Tsutsugamushi Fever.—Levine says that an investigation of the cardiovascular status of 130 patients convalescent from tsutsugamushi fever, made at a United States Army general hospital, showed no evidence of persistent myocardial damage. In its effect on the heart this disease seems to resemble diphtheria. If the patient survives the acute phase his heart eventually shows complete return of function. The disability following the acute phase of the disease is largely that of neurocirculatory asthenia. The disease is associated in its acute phase with a generalized vasculitis, which is followed by a state of poor vascular tone. The latter, rather than cardiac involvement, is believed to account for the poor response to exercise in the convalescent stage.

Typhoid in Immunized Subjects.—Tullis states that protection against typhoid by immunization is relative. The typhoid he observed in the 7 previously immunized subjects was atypical and difficult to diagnose. Abdominal pain was a prominent admission complaint. The Widal test was of limited diagnostic value, owing to the universal immunization of all subjects. Four patients in whom falsely positive (anamnestic) reactions were repeatedly demonstrated were also studied. The presence of a rising titer of agglutination was of no aid in differentiating the true from the false positive Widal reactions. Separation of the agglutination into the flagellar and somatic fractions was of limited diagnostic import. Positive flagellar agglutination occurred in both the patients with and the patients without typhoid. Somatic agglutination occurred in only the patients with typhoid. The clinical course seemed mild; the complication rate, however, was high. Complications included (1) transient icterus, (2) colon bacilluria, (3) clinical relapse and (4) perforation of the gallbladder, with peritoneal abscess formation and peritonitis. The treatment of all patients was symptomatic and consisted in high caloric diet and good nursing care. The recovery rate was 100 per cent.

7:143-208 (March) 1945

Influence of Crowding on Respiratory Illness in Large Naval Training Station. B. B. Breese, J. Stanbury, H. Upham, A. J. Calhoun, R. L. Van Buren and A. S. Kennedy.—p. 143.
Absence Without Leave: Psychiatric Study of 100. D. B. Davis, H. M. Wolman, R. E. Berman and J. E. Wright.—p. 147.
Physiologic Abnormalities and Pathologic Changes Following Exposure to Simulated High Altitudes. A. F. Goggio and G. H. Houck.—p. 152.
Nervous System Dysfunction in Adaptation to High Altitude and as Postflight Reactions. G. A. Brown, C. H. Cronick, H. L. Motley, E. J. Kocour and W. O. Klingman.—p. 157.
*Acute Heart Failure Following "Blast Injury." B. S. Leavell.—p. 162.
*Stability and Activity of Penicillin in Solution and in Ointment. J. S. Gots and A. M. Glazer.—p. 168.
Penicillin Program at the United States Naval Hospital, Portsmouth, Va.: Observations and Results. H. J. Fox.—p. 170.
*Visceral Leishmaniasis: Report of 3 Cases of its Occurrence in Members of the Armed Forces of the United States. J. H. Burchenal and R. P. Woods.—p. 173.
Simple Technic for Outlining the Sweat Pattern. J. J. Silverman and V. E. Powell.—p. 178.
Healing of Wounds in New Guinea. R. V. Byrne.—p. 181.

7:209-274 (April) 1945

Cornell Service Index: Method for Quickly Assaying Personality and Psychosomatic Disturbances in Men in Armed Forces. A. Weider, K. Brodman, Bela Mittelmann, D. Wechsler and H. G. Wolff, with technical assistance of Margaret Meixner.—p. 209.
Id.: Report of Its Use in Evaluation of Psychiatric Problems in Naval Hospital. N. Warner and Margaret W. Gallico.—p. 214.
Three Years of Naval Selection: Retrospect. C. L. Wittson and W. A. Hunt.—p. 218.
Field Nutritional Laboratory. R. E. Johnson.—p. 222.
Assessment of Nutritional and Metabolic Condition in Field: General and Clinical Aspects. R. E. Johnson, F. Sargent, P. F. Robinson and F. C. Consolazio.—p. 227.
Notes on Care of Battle Casualties: War Department Technical Bulletin.—p. 234.

Heart Failure Following "Blast Injury."—In the Italian campaign the majority of blast injuries in patients admitted to evacuation hospitals were due to land mines and high explosive shells, while only a small percentage developed from bombs. Most of these men had penetrating wounds, usually compound fractures of an extremity. Leavell observed 3 patients with blast injury presenting unexplained heart failure. All 3 were healthy young adults who had performed strenuous work until they were wounded. In none was there evidence of valvular disease; hypertension, renal disease or urinary suppression. The amount of fluid administered parenterally did not appear to be excessive. The fact that all 3 patients received a blast injury at the time of wounding and that heart failure developed several days later suggested the possibility that the two might be related. In an attempt to determine the factors responsible for the heart failure 35 other patients with blast injury were studied from a cardiovascular point of view. Two of these had abnormal venous pressures without obvious cause, and 3 additional

patients manifested electrocardiographic abnormalities. No adequate explanation can be offered for these observations. It is suggested that, when pulmonary edema develops following blast injury, digitalization and venesection may be indicated.

Stability of Penicillin in Solution and Ointment.—Gots and Glazer studied the activity and stability of penicillin in solution and in ointment bases by means of modifications of the agar plate assay and the serial dilution turbidity method. A solution and ointments of penicillin containing equal numbers of units showed practically the same activity. When the solution and the ointments were kept at refrigerator temperature there was no significant loss of activity at the end of sixty days. At room temperature and at incubator temperature there was complete loss of activity in approximately a month.

Visceral Leishmaniasis in the Armed Forces.—Burchenal and Woods draw attention to the occurrence of kala-azar among troops returning from the Mediterranean area. Kala-azar is characterized by the invasion of the reticuloendothelial system by a protozoon parasite, Leishmania donovani. The symptoms are long continued fever, oftentimes with a double daily elevation of temperature, and progressive splenomegaly followed by hepatomegaly, loss of weight, leukopenia and anemia. Generalized lymphadenopathy is occasionally noted. The authors present the histories of 3 patients whom they treated during the past three months. The first case is notable for the acuteness and severity of the disease and of the difficulty in establishing the diagnosis by demonstration of the parasite. The second shows a more chronic course but again illustrates the difficulty in finding the parasites. The third case presents an entirely different clinical picture, with moderate enlargement of the posterior cervical lymph nodes as the only sign of the disease. The first 2 patients responded to what is usually considered adequate treatment, but both relapsed shortly thereafter and required further therapy. The third patient is still undergoing treatment. Sternal aspiration is probably the safest method of demonstrating the leishmania parasites and should be tried first, but in some cases it may be necessary to resort to splenic puncture. Early diagnosis and institution of treatment before the occurrence of granulocytopenia is most important. Visceral leishmaniasis was first treated with antimony and potassium tartrate, and this agent may still be used where less toxic drugs are not available. The pentavalent antimony derivatives, such as neostibosan, neostam and sodium antimony gluconate, are less toxic.

Western J. of Surg., Obst. & Gynec., Portland, Ore.

53:93-134 (April) 1945

Penicillin in Treatment of Infections. C. S. Keefer.—p. 93.
*Sodium Penicillin in Treatment of Presumably Sulfonamide Resistant Female Gonorrhea. Paula Horn and H. H. Cowper.—p. 108.
Analysis of Unusual Rh Antibody. Joan Howard, Barbara C. McIvor and S. P. Lucia.—p. 113.
Radical Duodenopancreatectomy in One Stage for Carcinoma of Ampulla of Vater: Report of Case with Successful Outcome. J. R. Broun.—p. 118.

Sodium Penicillin in Sulfonamide Resistant Gonorrhea.—Horn and Cowper administered penicillin to 71 women with gonorrhea. All except 1 had received but had failed to respond to one or more courses of sulfonamide treatment. The remaining patient had been started on penicillin because she had nonspecific hepatitis. The sodium penicillin was administered at three hour intervals by intramuscular injection in sterile distilled water or in isotonic solution of sodium chloride. The individual doses varied between 20,000 and 50,000 units and the total doses ranged from 100,000 to 200,000 units. More than one fifth of the women failed to respond to the penicillin therapy. Among the 43 women who had involvement of only the lower genital tract 5 failed to respond to penicillin, but of the 31 with associated upper genital tract infection 11, or more than a third, failed to respond. The authors also observed the trend that the older was the infection, the poorer was the chance of success with penicillin in the dosages used. They stress that early diagnosis and early institution of penicillin therapy are paramount considerations in the control of gonorrhea. In the female, in whom diagnosis and cure are difficult to establish and time consuming, delay caused by a preliminary trial with the sulfonamide drugs may diminish the possibility of cure.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

57:1-44 (Jan.-Feb.) 1945

*Skin Eruptions Due to Local Application of Sulfonamides. G. A. G. Peterkin.—p. 1.
Incidence and Localization of Acne. E. L. Cohen.—p. 10.

Skin Eruptions from Local Application of Sulfonamides.—Peterkin directs attention to the skin eruptions that have been known to follow the local application of the sulfonamides. He observed a number of these cases in 1942 in England and 65 cases in North Africa in 1943, many of them of much greater severity than those seen in England. In 61 of the 65 cases sulfanilamide powder was the first sulfonamide drug to be applied. The eruption is invariably preceded by application of the powder, and it is suggested that the patient becomes sensitized to the drug by its inhalation. It is recommended that powdered sulfonamides should not be applied to the skin for minor conditions. Over 200 patients, including 183 with impetigo or impetiginized seborrheic dermatitis, were treated in North Africa with 5 per cent sulfathiazole in Lassar's paste or Lanette wax cream, and the skin freely exposed to light. Only 1 patient (with respirator dermatitis) developed an eruption; this was mild and soon subsided. It is considered that 5 per cent sulfathiazole in a suitable base is probably as safe as ammoniated mercury for dermatologic therapy and gives better results.

British Journal of Venereal Diseases, London

21:1-46 (March) 1945

Venereal Diseases in Soviet Union. J. A. Scott.—p. 2.
Secondary Reaction in Twenty Day Intensive Arsenotherapy. R. H. Grede.—p. 9.
Social Aspect of Venereal Diseases: I. Work of Almoner. Dorothy M. Manchée.—p. 12.
Id.: II. Contact Tracing and Prostitute. Margaret A. Wailes.—p. 15.
Id.: III. Contact Tracing. Hilda M. Johns.—p. 17.
"Middle East Granuloma": Is it Granuloma Venereum? W. R. S. Cowe.—p. 34.

British Medical Journal, London

1:285-318 (March 3) 1945

*Cross Infection Risks in Hospitalization of Measles Patients. J. Wright.—p. 285.
Changes in Personality After Cerebrospinal Fever. M. N. Pai.—p. 289.
Psychiatric Casualties in Women's Service. S. I. Ballard and H. G. Miller.—p. 293.
Ludwig's Angina. J. Farr and E. D. Stanhope.—p. 295.
Inguinal Hernia in Merchant Navy: Analysis of 200 Consecutive Cases. P. P. Cole.—p. 296.

Cross Infection Risks in Hospitalization of Patients with Measles.—Wright found that almost three fourths of 65 patients with measles in one group became cross infected with type 6 hemolytic streptococci. Twelve of these patients developed middle ear suppuration and 4 were subjected to mastoid operations. More than a fourth of the patients developed skin infections, mainly impetigo. In another group analysis was made of the occurrence of middle ear suppuration among all the patients with measles hospitalized between December 1942 and May 1943. Among 496 patients 3.6 per cent suffered from "early" and 13.3 per cent from "late" middle ear suppuration. In view of the findings in the first investigation it could be assumed that the great majority of the late middle ear complications were due to cross infection. The late middle ear suppuration rate was considerably lower among patients admitted in April and May than among those admitted in the winter months. The percentage incidence of ear complications was not higher among children under 3 years of age, but the seriously damaging effects of cross infection fell most heavily on them. Of the 238 children in this group, 11 underwent mastoidectomy and 1 died. Infants under 1 year of age suffered particularly severely; 6 of the 45 infants developed late middle ear suppuration, and in 4 cases this was followed by further complications. In view of the high complication rate due to cross infection, treatment at home rather than in the hospital is advocated for patients with uncomplicated measles. For the

protection of measles patients who must be admitted to the hospital recommendations are made for the control of cross infection and for improvements in administrative and nursing procedures.

Edinburgh Medical Journal

12:1-48 (Jan.) 1945

Prophylaxis from Obstetric and Gynecologic Standpoint. R. W. Johnstone.—p. 1.
Traumatic Ulnar Neuritis: Results of Anterior Transposition of Ulnar Nerve. R. L. Richards.—p. 14.
Comparison of Pathogenicity Tests for Staphylococci. R. Salm.—p. 22.
Thiouracil in Treatment of Thyrotoxicosis. D. M. Dunlop.—p. 30.

Lancet, London

1:263-294 (March 3) 1945

Value of Work in Treatment of Tuberculosis. F. Heaf.—p. 263.
Exfoliative Dermatitis Treated with Cystine: Report of 2 Cases. B. A. Peters.—p. 264.
Nitrogen Loss After Thermal Burns: Effects of Adding Protein and Methionine to Diet of Rats. P. B. Croft and R. A. Peters.—p. 266.
Uterine Graft Operation for Genital Prolapse. T. C. Clarke.—p. 272.
Fatigue Fracture of Fibula: Report of 2 Cases. D. A. Richmond.—p. 273.

1:295-326 (March 10) 1945

Medicine and the State. L. Horder.—p. 295.
Dehydration. D. A. K. Black.—p. 298.
*Experimental Nephrosclerosis: Prevention with Ammonium Chloride. H. Selye, O. Hall and E. M. Rowley.—p. 301.
Reaction After Pneumoperitoneum Treatment. E. Aslett and T. F. Jarman.—p. 304.
Periarteritis Nodosa Possibly Due to Sulfadiazine Sensitivity. B. D. Rosenak and R. H. Maschmeyer.—p. 305.

Ammonium Chloride for Experimental Nephrosclerosis.—Selye and his associates point out that desoxycorticosterone acetate produces nephrosclerosis and hypertension in many animal species, especially if given to unilaterally nephrectomized animals kept on a high sodium chloride intake. The authors report experiments on rats which indicate that ammonium chloride is highly effective in preventing some of the most serious toxic effects of overdosage with desoxycorticosterone acetate. Since there is reason to believe that nephrosclerosis with renal hypertension, periarteritis nodosa and perhaps also some of the manifestations of "rheumatic fever" are due to intoxication with excessive amounts of an endogenous cortical substance resembling desoxycorticosterone acetate, it seemed desirable to examine the efficacy of ammonium chloride in patients with such diseases. This salt may also make it possible to use desoxycorticosterone acetate more extensively in adrenal cortex deficiency without incurring the danger of overdosage. This would be a new application of a remedy which has been used in large doses as an expectorant and diuretic and would not necessitate the extreme caution necessary with a new drug.

1:327-358 (March 17) 1945

*Decortication in Clotted and Infected Hemothoraces. C. P. Thomas and W. P. Cleland.—p. 327.
X-Rays in Diagnosis and Localization of Gas Gangrene. F. H. Kemp.—p. 332.
Iron Oxide Dust and Lungs of Silver Finishers. A. I. G. McLaughlin, J. L. A. Grout, H. J. Barrie and H. E. Harding.—p. 337.
Mite Borne Typhus in Anglo-Egyptian Sudan. R. W. Stephenson.—p. 341.

Decortication in Clotted and Infected Hemothoraces.—According to Thomas and Cleland, hemothorax is by far the commonest complication in chest injuries. The compound hemothorax which is associated with injury to the lung, diaphragm or chest wall requires surgical treatment, and the associated hemothorax if removed at the time of operation rarely causes further serious trouble. The simple hemothorax presents a different problem. Its mortality and morbidity depend almost entirely on infection or clotting. The increased incidence of massive clot formation observed in casualties from the Western European campaign may possibly be due to the employment of intrapleural penicillin, but in vitro experiments have lent no support to this view. The extensive use of intrapleural penicillin has unfortunately been associated with a tendency to disregard the principles of early and frequent aspiration of blood from the pleural cavity, so that many cases remain virtually unaspirated for a considerable period. An additional factor may be the high proportion of mortar wounds resulting in increased tissue damage. Among the 750 patients with chest injuries observed by the authors, 526 had hemothoraces. Of these, 30 per cent became infected and in 9 per cent clotting resulted. Earlier methods of treating clotted hemothoraces were attended by incomplete or considerably delayed lung expansion; at the best such methods led to considerable respiratory embarrassment. Less fortunate cases were left with severe and prolonged pleural infection. The employment of decortication with suction drainage fulfils the basic principle of early and complete reexpansion of the lung. Results in a limited series of hemothoraces have been considerably better than those of earlier procedures. A small series of both drained and undrained empyemas following hemothoraces have also been treated successfully by decortication and suction drainage.

Medical Journal of Australia, Sydney

1:129-164 (Feb. 10) 1945

Sterility. F. A. Bellingham.—p. 129.
Effort and Result in Sterility: Audit of 407 Cases. A. Grant.—p. 134.
General Aspects of Sterility in Female. J. W. Johnstone.—p. 138.
Hysterosalpingography in Sterility. C. MacDonald.—p. 142.
Examination of Semen. H. F. Bettinger.—p. 144.

1:213-240 (March 3) 1945

Intestinal Intubation. J. Devine.—p. 213.
Further Report on Treatment at Children's Hospital, Melbourne, of Influenzal Meningitis with Sulfonamides and Type Specific Serum. Elizabeth K. Turner.—p. 219.
"Found Dead," "Dead in Bed," and "Collapsed and Died." J. B. Cleland.—p. 221.
*Hemiaplasia of Thyroid Gland. H. R. G. Poate and S. L. Spencer.—p. 223.
*Case of Chronic Solid Subdural Hematoma. R. A. Money.—p. 224.

Hemiaplasia of Thyroid.—Poate and Spencer report 2 cases of hemiaplasia of the thyroid. The anomaly occurs often enough to require the surgeon to expose both sides before beginning a thyroidectomy. The danger of inadvertently removing the patient's entire thyroid tissue is increased by the fact that in the great majority of cases of hemiaplasia it is the left lobe which fails to develop. In both of the cases recorded here the left lobe was lacking. As it is almost universal practice in thyroid surgery to begin on the right side, the operator may detach this lobe from its vascular supply before becoming aware of the absence of the left lobe.

Solid Subdural Hematoma.—According to Money, solid subdural hematoma is rare. A man aged 23 presented symptoms suggestive of the presence of a cerebellar tumor on the left side. Preparations were begun for an exploratory suboccipital operation. As a preliminary step, burr holes were made in the skull over both occipital lobes. On the left side the dura mater was thick and discolored, and, when it was cut through, brown fluid and old liquid blood escaped, indicating the presence of an old subdural hematoma. About an ounce of liquid was evacuated by lavage and suction, with immediate relief of symptoms, and a small piece of corrugated rubber was inserted in a forward direction. It was hoped that the remainder of the hematoma would drain out this way. After the discovery of the hematoma, the patient recollected that about the end of March 1942, while playing soccer, he had received a blow or kick on the head, which knocked him down. He continued the game for at least half an hour in a dazed condition; yet this minor injury must have been sufficient to tear one of the cerebral veins entering the sagittal sinus and start bleeding into the subdural space. Later the patient had a generalized epileptic seizure; the headaches persisted and papilledema increased. These and other observations made it obvious that a large, probably clotted and organized subdural hematoma was still present. After a large osteoplastic flap had been raised and the thickened dura reflected, a substance having the appearance of liver was encountered in all directions. This liver-like mass represented a solid subdural hematoma. The patient made a good recovery.

Proceedings of Royal Society of Medicine, London

38:97-140 (Jan.) 1945. **Partial Index**

Physical Preparation of Commandos. G. M. Levick.—p. 97.
Discussion on Influence of Nutritional Factors in Liver Disease. H. P. Himsworth, L. E. Glynn, J. Beattie and C. Wilson.—p. 101.
Spinal Analgesia in the Very Young and Further Observations. W. Etherington-Wilson.—p. 109.
Serial Spinal Analgesia. J. A. Lee.—p. 115.

Semana Médica, Buenos Aires

52:223-270 (Feb. 1) 1945. **Partial Index**

*Sulfonamide in Therapy of Trichomoniasis Vaginalis. A. Alexander. —p. 248.

Sulfonamide Therapy of Trichomoniasis Vaginalis.—Alexander describes the local sulfonamide treatment of 26 patients with trichomoniasis vaginalis. The vagina was washed with 1 liter of boiled water and was cleansed with sterilized gauze, a sulfonamide tablet was placed in each cul-de-sac and the vagina was tamponed with gauze. The treatment was repeated on five or six consecutive days. The discharge, the vulvar pruritus and the burning local sensation disappeared after the first day in the course of the treatment. The permanent disappearance of the flagellum was verified by microscopic examination of the discharge.

Chirurg, Berlin

16:1-50 (Jan.) 1944. **Partial Index**

*Electrocoagulation of Gasserian Ganglion. K. H. Bauer.—p. 1.
Adhesive Pericarditis. E. K. Frey.—p. 5.
Arteriography in Frostbite. B. Breitner.—p. 8.
Management of Craniocerebral War Injuries. W. Kufferath.—p. 10.
Pathology and Clinical Aspect of Cerebral Abscess After Cranial Gunshot Injury. J. E. Lemke.—p. 16.
Exploratory Excision of Capsule in Suspected Tuberculosis of Knee Joint. H. D. Schumann.—p. 27.

Electrocoagulation of Gasserian Ganglion.—Bauer reports experiences with electrocoagulation of the gasserian ganglion in more than 500 cases of neuralgia. There was not a single fatality. Injection of procaine hydrochloride solution is made to infiltrate the track for the puncture cannula to the base of the skull. A 12 cm. long, thin cannula insulated with celluloid is introduced and is passed slowly forward along the foramen ovale without touching the base. The passage through the foramen ovale is made manifest by sudden radiating pain in the area of the third branch and by resistance offered by the nerve. X-ray examination of the position of the needle prior to coagulation is imperative. Examination of the eyes is important because changes in vision, in the size of the pupils and in the ocular movements suggest that a change in the position of the needle is required. This may also be necessitated by aspiration of blood or cerebrospinal fluid or by nausea. After these precautionary measures, high frequency electrocoagulation with the alternating current may be performed under evipal sodium anesthesia. Coagulation should be made in four stages of fifteen, twenty, twenty-five and thirty seconds' duration. The intensity of the current is increased during the last stage. Coagulation itself should not be performed under local anesthesia. Residual pains may persist for two or three days. Electrocoagulation may be repeated when pain persists on the fifth or sixth day, as well as in recurrences. The advantage of the method is that the effect of the current is limited to the area immediately next the cannula, thus preventing severe destruction at the base of the skull or extensive bone sequestration in the area of the base and of the upper jaw.

Deutsche medizinische Wochenschrift, Leipzig

70:23-52 (Jan. 21) 1944

Disturbances of Auditory Apparatus and of Apparatus Concerned with Maintaining Equilibrium and Inflammatory Disorders of Ear in Typhus. L. B. Seiferth.—p. 23.
So-Called New Infectious Diseases. J. Mrugowsky.—p. 24.
*Sulfonamide Therapy of Malignant Diphtheria, with Special Reference to Typhus Associated with Diphtheria. Harmsen and Siegler.—p. 27.
Treatment for Sciatic Neuralgia with Injections. E. Vaubel.—p. 28.
Problem of Active Immunization Against Scarlet Fever. E. Hässler. —p. 30.
Serum Therapy of Multiple Sclerosis. W. H. A. Schöttler and H. Seibach.—p. 32.
Experimental Study on Pathogenesis and Therapy of Intestinal Autointoxication. H. Nicolai.—p. 34.
Clinical Diagnosis of Myeloma (Plasmocytoma). F. Leypold.—p. 36.
Clinical Course of Otitis Media. R. Mittermaier.—p. 38.
Pathology of Round Ulcer During First Year of Life. H. Mellerowicz. —p. 41.

Sulfonamide Therapy of Typhus and Diphtheria.—Harmsen and Siegler report experiences with sulfonamide therapy in 30 severe toxic cases of diphtheria and in 23 cases of typhus complicated by diphtheria. Intravenous injections of large doses of sulfaethylthiazole (7 to 8 Gm.) were given for two to three days. Rinsing of the mouth and of the throat with a 3 to 5 per cent solution of sulfaethylthiazole was practiced at the same time. Rapid shrinking of false membranes took place and the membranes were cast off within three to four days. Edema of the throat subsided rapidly. Smears became negative within a short time. Sulfaethylthiazole was particularly effective in cases of mixed typhus and diphtheria infection complicated by pneumonia. The mortality rate was reduced from 80 per cent to 30 per cent.

Münchener medizinische Wochenschrift, Munich

91:271-296 (June 2) 1944. **Partial Index**

Treatment of Diabetes Mellitus in War. K. Gutzeit.—p. 271.
Front Line Surgery. E. Melzner.—p. 274.
*Full Diet in Diabetes Mellitus. H. J. Banse.—p. 276.
Commotio Cerebri and Mechanonarcosis as Effects of Increased Intracranial Pressure. U. Ebbecke.—p. 280.
Chemotherapy with Sulfonamides in Surgery: Critical Considerations and Personal Experiences. E. Grau.—p. 282.
Resumption of Work under Medical Supervision by Patients with Tuberculosis of Lungs as Necessary Preparation for Definite Return to Work. R. Griesbach.—p. 284.
*"Vegetative Insulin Shock" in Treatment of Urticaria. H. Bartelheimer. —p. 286.

Full Diet in Diabetes Mellitus.—Food conditions in Germany prompted Nonnenbruch to suggest that patients with diabetes mellitus should be granted the same rations as normal persons. According to Banse, change in metabolism for the worse resulted from a full diet consisting of unlimited carbohydrates and of normal small rations of fats and proteins with the addition of sugar and sweet marmalade. Results with limited diet consisting of unlimited carbohydrates without the addition of sugar were on the average satisfactory. Of 1,200 patients with diabetes 228 were given a full or limited full diet. Experiments were carried out on 170 men and on 58 women of various age groups as well as on children. The limited full diet was well tolerated by 136 (114 men and 22 women), i. e. 11.3 per cent of the total of 1,200 patients. Insulin was administered simultaneously to 96 patients (82 men and 14 women), whereas 40 (32 men and 8 women) did not require insulin. These 96 patients had "island diabetes"; they did not present symptoms of severe endocrine disturbances of metabolism. Insulin treatment was effective, the blood pressure was normal and there was no tendency either to obesity or to emaciation. The fasting blood sugar values of the 40 patients not on insulin treatment were up to 130 and 140 mg.; there was a mild glycosuria independent of the food, so that the terms diabetes lenissimus and diabetes innocens could be applied to them. The dose of insulin required in cases in which a prolonged limited full diet proved satisfactory was not higher than that of patients on a diabetic diet. Normal carbohydrate tolerance could not be produced in patients with diabetes mellitus by the administration of insulin. On limited full diet the normal work capacity could be maintained and a change of metabolism for the worse could be prevented in only a small portion of men. In all other patients, particularly in women, a sufficient metabolic balance could be maintained only on a diet which took into account the reduced carbohydrate tolerance.

"Vegetative Insulin Shock" in Treatment of Urticaria.—Bartelheimer treated with insulin several hundred cases of acute urticaria. Hypoglycemia characterized by vegetative symptoms can be produced by subcutaneous administration of 30 to 40 units of insulin. The rash subsides promptly with the outbreak of sweat and the occurrence of tremor, fatigue and palpitation. The more pronounced the vegetative symptoms of the insulin shock, the better the effect of the treatment. Intravenous injections of 10 to 16 units of insulin are suggested. Attention to the normal function of the kidneys and the pituitary is important in order to prevent severe hypoglycemia. The risk of circulatory failure has been overestimated, but electrocardiographic examination should be carried out prior to insulin administration in cases of rash following administration of diphtheria or scarlet fever serum. Satisfactory results were obtained with insulin shock treatment in these specific cases. Intravenous administration of the drug is not advisable in these cases and in hypotension. The treatment is likewise effective in chronic urticaria with repeated administration of small doses of insulin once or twice a day.

Book Notices

Foundations of Neuropsychiatry. By Stanley Cobb, A.B., M.D., Bullard Professor of Neuropathology, Harvard Medical School, Boston. Third edition. Cloth. Price, $2.50. Pp. 252, with 13 illustrations. Baltimore: William Wood & Company, 1944.

The popularity and usefulness of Dr. Cobb's book is attested by the fact that it is now in its third edition. It is surprising to note how well the author has performed his task of simplifying and schematizing a complex subject. In doing so he has of course subjected himself to the criticism of eliminating much important material and of being guilty of dogmatic assertions when these are not possible. It is difficult to see how these can be avoided in attempting to present neurology to medical students, and it should be borne in mind that to simplify adequately presupposes a sound knowledge of the subject in question. In this regard the author qualified without question. To follow the opposite extreme would be to make the subject both unpalatable and unintelligible. Despite the pitfalls inherent in his chosen approach to the problem of neuropsychiatry, Dr. Cobb has succeeded admirably in writing a book which does indeed present the essential features of a complex branch of medicine.

It is gratifying to note that although the author has always been a sound advocate of the inseparability of structural and psychogenic processes he has not found it necessary to resort to psychosomatics as a new form of psychiatric thinking. His little volume is testimony to the fact that psychosomatics has always occupied those neuropsychiatrists with a broad vision of their field.

The chapter on special neuropathology would have been more useful if it had been confined to a general discussion of neuropathologic processes such as demyelination and infection. Its consideration of the special diseases is too brief to be really useful. The chapter on psychopathology is subject to the same criticism. It would seem better to have confined the discussion of this problem to general concepts than to have attempted thumbnail sketches of diseases.

There has been added in this edition a new chapter on psychology which discusses briefly such problems as the instincts, intelligence, memory and attention. It is much too brief to cover the subject adequately, but it is useful in that it provides a springboard for further reading and presents a point of view on which further knowledge can be based. This is probably the most important feature of Dr. Cobb's book, that it provides a background and point of view which can be expanded or contracted as the student desires. There can be no hesitation in recommending the book highly not only to medical students but to all those who contemplate choosing neuropsychiatry as their field of choice.

Modern Methods of Amputation. By Edmundo Vasconcelos, Professor, University of São Paulo. With an Introductory Survey of the Development of Amputation by Major Gen. Norman T. Kirk, M. C., Surgeon General, U. S. Army. Fabrikoid. Price, $10. Pp. 253, with 258 illustrations. New York: Philosophical Library, Inc., 1945.

This volume contains information valuable to any practitioner who may be faced with a problem of amputation surgery. The general principles of amputation are well stated. The distribution of skin flaps, the handling of muscle and fascia, the treatment of bone, with emphasis on respect for periosteum and the treatment of the nerve trunks, are all clearly and soundly stated in the text. Some of the instruments for and methods of retraction, which are so well illustrated, will however in unskilled hands lead to great stripping of the periosteum. Their hazards are not stressed.

The levels of amputation are cleverly and strikingly illustrated. As stated for the upper extremity, no exception can be taken. As stated for the lower extremity the level of 5 centimeters below the middle of the calf for an ideal below the knee amputation stump is open to question. This is considerably longer than the American prosthesis maker likes to fit and is in an area of the calf which is likely to have poor circulation and ulcerate easily.

The technics for individual amputations are well described, particularly the technic of the Syme-Ollier amputation, in which the author stresses the vulnerability of the blood supply to the flap and its protection by subperiosteal stripping of the os calcis. No other modern treatises on amputations cover well the pitfalls in this valuable procedure.

The paragraphs on interscapulothoracic amputation and disarticulation of the hip are in great detail and effectively illustrated in a manner to make the anatomy clear. Other modern textbooks on amputation leave much to be desired concerning these very major operations, which this volume makes clear.

The extensive description of the various modifications of amputations of the osteoplastic type through the astragalus and os calcis, including an original operation by the author, is interesting and is of value to the expert in amputations. However, the simplicity with which they are presented is likely to lead the average surgeon into procedures which will result unsatisfactorily. The successful selection of patients for these types of procedure and the execution of the operation require considerable experience in bone surgery, and these procedures should not be carried out by even the greatly experienced soft tissue surgeon.

The chapter on prosthesis is an outline and should be more detailed. While the important elements in after-care of the stump, viz. massage, active exercise, elimination of contractures and muscular development, are all mentioned briefly, there is much detail of this important aspect of rehabilitation which could be included and stressed with benefit to both practitioner and patient. No mention is made of the importance of teaching from the beginning proper walking habits, the technic of which is extremely important to the ultimate result of the surgery.

A chapter on the immediate complications of the surgery, viz. shock, hematoma, infection, necrosis of skin flaps and their management, would be a valuable addition toward completeness.

The illustrations are well done and informative and they stress the anatomic aspects of the operative procedures. All however show clearly an unnecessarily extensive undermining of the skin in the subcutaneous plane, which in some instances will result in the complication of necrosis of the skin flaps.

This book is one from which the expert, the practitioner who occasionally does an amputation and the student can all get ideas. It is a valuable addition to the literature on this phase of surgery and should be in every surgical library.

Colloid Chemistry Theoretical and Applied. By Selected International Contributors. Collected and Edited by Jerome Alexander. Volume V: Theory and Methods, Biology and Medicine. Cloth. Price, $20. Pp. 1,256, with illustrations. New York: Reinhold Publishing Corporation, 1944.

This large volume covers the "more recently developed theories, methods and procedures, as well as new topics or newer aspects of old topics" in colloid chemistry. The book is divided into two major portions. It is unfortunate that the second part (Biology and Medicine) could not have been published separately, for the first section will not appeal to the medical profession as a whole.

The first part (Theory and Methods), consisting of twenty-five chapters, includes descriptions and discussions of methods for the analysis of complex molecular structures with the aid of x-rays, the electron microscope (which includes some fine photographs of micro-organisms), high vacuum distillation, polymerization, sonic and ultrasonic waves in colloid chemistry, the cyclotron and some of its uses (especially in biology and medicine), electrophoretic studies of proteins and related substances (with part devoted to the electrophoretic study of blood, hormones, serums and numerous references to its use in other biologic studies). This section, as a whole, is written in a highly technical vein appreciated by the physicist, chemist or engineer but outside the ken of most medical practitioners.

The second portion of the book is also technically presented but obviously within the grasp of the physician. Articles covering the following subjects are presented: proteins; catalysis as a biologic factor; photosynthesis; plant cell membranes; recent advances in starch chemistry; enzymes and the biologic action of vitamins; minerals and vitamins in applied nutrition; mechanism of hormone action; molecular organization of visual processes; chemical pacemakers and physiologic rhythms; colloid chemistry of purified viruses; the gene as a structure of colloidal dimensions; the gene as a chemical unit; colloid chemistry in embryonic development; physical states of protoplasm compatible with life; physical properties of protoplasm; surface-

chemical properties of protoplasmic proteins; physical change of muscle related to activity; capillary circulation; biochemical and physiologic mechanisms in inflammation; modern outlook on blood coagulation; immunology; allergy and anaphylaxis; homeostasis (the maintenance of steady states in the organism); causes and nature of cancer; gerontology; formation of concretions; aero-emphysema and caisson disease; action of war gases; infective aerosols; physical chemistry of lipids, physicochemical mechanisms in neuropsychiatric disorders; psychiatry; changes in the surrounding medium produced by free living cells; physicochemical basis of organic evolution. Each chapter carries an extensive reference list.

These chapters are written by workers who are generally recognized as authorities in their respective fields. Such names as C. A. Elvehjem, Oliver Kamm, W. M. Stanley, Robert Chambers, Otto Meyerhof, William C. Boyd, Carl A. Dragstedt, Walter B. Cannon, Leo Loeb and A. J. Carlson constitute only a partial but representative list of the authors.

In addition to his knowledge and organizational ability, one of the editor's chief assets lies in his capacity to point out the significance of experimental data and present it in the proper perspective relative to the general pattern of biologic science.

The second half of the book is certainly of great value and interest to the physician, for it correlates and integrates physiologic and biochemical actions with the phenomena of living processes. In the various articles the doctor is given an opportunity to reacquaint himself with, or to learn of, new facts and theories on numerous subjects, each presented in relatively few pages.

The Pathology of Internal Diseases. By William Boyd, M.D., LL.D., M.R.C.P., Professor of Pathology and Bacteriology in the University of Toronto, Toronto. Fourth edition. Cloth. Price, $10. Pp. 857, with 374 illustrations. Philadelphia: Lea & Febiger, 1944.

This edition has been brought up to date with particular reference to such subjects of current interest as primary atypical pneumonia, Q fever, blast injury, Meigs's syndrome, dietary cirrhosis of the liver, infective hepatitis, alloxan diabetes, crush nephritis, sulfonamide nephritis, the Rh factor, sarcoidosis and equine encephalomyelitis. The discussion of diseases of the cardiovascular system has been amplified, and various other sections have been rewritten "in part or in whole." Twenty-two new black and white illustrations and four new colored plates have been added. The value of this book rests mainly on its correlation of symptoms with pathologic lesions, thus making pathologic anatomy the keystone of clinical medicine. As the author said in the first edition, this book is meant to be essentially "an illustrated textbook of internal medicine written from the point of view not of diagnosis or of cure but of the mechanisms of disease, its why and its wherefore." Although the book is of particular value to medical students studying special pathology, it should be of equal value to clinicians who wish to keep abreast of advances in clinical medicine. The discussions are necessarily brief, but the author's ability to condense and the excellent illustrations make the reading easy. The book should continue to serve well its original purpose.

An Experiment in Applied Nutrition for Canadian Communities. Summary Report of the Swift Fellowship. By Edna M. Guest, O.B.E., M.D., and Miss Ethel Chapman. Paper. Pp. 192. Toronto: Trustees of the Swift Fellowship, 1944.

This is the report of the work carried on in the year 1942-1943 under a fellowship providing for visits by a home economics nutritionist to local communities of all sections of Canada. In each town conferences were held with all available persons interested in or acquainted with nutritional problems such as public health nurses and doctors, teachers, women's clubs and nutrition committees. Encouragement and advice for planning nutritional improvement was given to individuals and groups. Plans were made for overcoming local food problems. Follow-up reports from the communities are given which show the achievements made as a result of the worker's visit. It was felt that in each case definite benefits were traceable to the personal visits made possible by the fellowship. This served to bridge a gap between the scientific sources of knowledge and its practical application.

Lições de anestesiologia: Curso realizado sob os auspícios da reitoria da Universidade de S. Paulo e da 2.ª região militar. Raul Briquet, editor. Com a colaboração de P. Aires Neto, et al. Boards. Pp. 490, with illustrations. São Paulo: Editora Atlas S. A., 1944.

The editor, with nineteen collaborators, has reviewed the literature in connection with the administration of anesthetics and has emphasized methods employed, particularly in the United States. Some of the subjects covered are the evolution of anesthesia and the effects of anesthetics on the central nervous, respiratory, circulatory, digestive and urinary systems. The chemistry and pharmacology of anesthetic agents are discussed, as are preliminary medication, surgical anesthesia for war, inhalation anesthetics and rectal, intravenous, spinal, peridural, local and regional anesthesia. Technical problems of anesthesia and the subject of respiratory obstruction and the postoperative complications are considered in detail. There are chapters on oxygen therapy and on gas anesthesia apparatus. This volume is evidence of great interest in anesthesiology in South America, especially in Brazil and in the University of São Paulo. Anesthesiologists will be impressed with the thorough comprehension of all the commonly used methods of anesthesia that are covered.

Functional Disorders of the Foot: Their Diagnosis and Treatment. By Frank D. Dickson, M.D., F.A.C.S., Associate Professor of Clinical Surgery, Medical School, University of Kansas, Kansas City, and Rex L. Diveley, A.B., M.D., F.A.C.S., Colonel, Medical Corps, Army of the United States. Second edition. Fabrikoid. Price, $5. Pp. 352, with 202 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1944.

In its second edition this work has undergone much improvement, with additions of chapters especially related to military and industrial phases of foot problems. As the title suggests, the routine foot problems confronting practitioners are resolved to their simplest terms by sound reasoning. Diagnoses are classified and treatment is outlined. Dignity is given to the entire foot problem. The book is recommended to all, especially the military, pediatrician and general practitioner. Numerous photographs and line drawings supplement the text. A well organized bibliography contains many references for supplemental reading.

Uncle Sam Convalescing: A Glimpse into His Hospital Record from 1933-1940. By H. Ameroy Hartwell, M.D. Cloth. Price, $2. Pp. 79, with 6 illustrations. Boston: Bruce Humphries, Inc., 1944.

"Uncle Sam Convalescing" is an interesting, original, economic case history and day by day hospital record of the first seven critical years of 1933 to 1940. Free use of charts, physical examination forms and summary sheets enable the reader to trace the rise and fall of pulse rate, blood pressure and general all around condition from the closing of the banks until Hitler and Mussolini began to show uncontrollable maniacal tendencies. Throughout the author deals with national events in the language of medicine which is amusing, surprising and entertaining, particularly in the early pages.

Notable Names in Medicine and Surgery. By Hamilton Bailey, F.R.C.S., Surgeon, Royal Northern Hospital, London, and W. J. Bishop, F.L.A., Sub-Librarian, Royal Society of Medicine, London. Cloth. Price, 15s. Pp. 202, with illustrations. London: H. K. Lewis & Co., Ltd., 1944.

Here are almost a hundred brief biographies, with photographs of great names in the history of medicine, particularly eponyms. The descriptions are brief. The great number of illustrations make the book especially living and delightful. Several Americans are included, notably Sims for the speculum, Bigelow for a ligament, McBurney for his point, Welch for his bacillus, Ochsner for his treatment of appendicitis, John B. Murphy for his drip, his sign and his button, Kelly for the proctoscope, and the Mayos for some operations and the scissors.

Alcoholics Are Sick People. By Robert V. Seliger, M.D., in collaboration with Victoria Cranford. Edited by Harold S. Goodwin, B.A. Cloth. Price, $2. Pp. 80. Baltimore: Alcoholism Publications, 1945.

This small treatise is one of the best on alcoholism. It is about time that the layman be made to recognize the fact that the abuse of alcohol is a psychiatric disease as well as any other disease and that the patients need treatment by a psychiatrist. The author's book actually does this. It is thoroughly honest and straightforward. It should be in the hands of all medical men and social workers.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TESTS FOR DRUNKENNESS

To the Editor:—**As assistant city physician I am interested to know the best ways to find out when a person is inebriated (drivers) so I can prove it in court. I bought a LaMotte set and had it used twice during the last fifteen days on the urine of intoxicated drivers. I just got my copy of Approved Laboratory Technic by Kolmer and Boerner and to my dismay I read on page 905 that the estimation of the amount of alcohol found in the urine is valueless. Please tell me how can I prove that a person is inebriated without having to anesthetize or kill him? Also please tell me the percentage of alcohol that should be in the urine of the person examined to be called drunk and the percentage in the four stages of acute alcoholism.** Jesus Chapa-Badillo, M.D., Laredo, Texas.

ANSWER.—This query is based on the following quotation from Kolmer and Boerner:

> It has been fairly well established that the various methods to determine intoxication, such as an estimation of the amount found in the urine or expired air, are valueless, since they are excreted and no longer causing inebriation. (Inebriation depends upon the amount of unoxidized alcohol in the brain.) Hence the ideal method is to determine the amount of alcohol present in the brain tissue. This of course is easy in the cases coming to necropsy but correspondingly difficult in an intoxicated individual. In such cases examination of the spinal fluid is probably of greatest value. For further details the reader must consult the enormous literature which has accumulated.

The assertions in this quotation are so obviously contrary to generally accepted opinions that Kolmer was asked to clarify the situation. He explained that the material under discussion had been written by a collaborator, who had based his opinions largely on the work of Gettler and his associates, and that this material had escaped revision. That Kolmer himself is in complete accord with the investigators who admit the importance of testing all body fluids is evident from quotations from his book Clinical Diagnosis by Laboratory Examinations (D. Appleton-Century Company, 1944):

> Ethyl alcohol intoxication may be detected also by tests conducted with the breath and urine. With the latter a concentration of less than 0.1 per cent produces no intoxication; mild intoxication may occur in about 50 per cent of individuals with a concentration of 0.1 to 0.2 per cent; moderate intoxication with 0.2 to 0.3 per cent, and marked intoxication with 0.4 per cent or higher.

These statements are documented with references to the literature, and a more complete discussion of concentrations of ethyl alcohol in the blood in relation to intoxication is given on pages 194 and 195. In 1931 Gettler and Freireich reported a closer relationship between brain alcohol and spinal fluid alcohol than between brain and blood alcohol, and they concluded that brain alcohol and spinal fluid alcohol furnish the only adequate chemical criteria for intoxication. Again in 1944 Gettler, Freireich and Schwartz reported additional information on blood and brain alcohol. They determined the blood-brain alcohol ratio in a series of 28 dogs that had been given alcohol by stomach tube. From their experiments they concluded that the alcohol in the blood and other body fluids varies so greatly from brain alcohol that these fluids are unsuitable for diagnosis of inebriation in man. This work is open to criticism from many standpoints. The method of analysis used accounts for from 83 to 89 per cent of the alcohol present, and yet the authors report their findings to the third decimal place—mathematical precision with insignificant figures. The extreme limits of brain-blood ratios in dogs were used to calculate possible variations in human brain alcohol based on blood alcohol determinations. The dog furnishing one of the extreme blood-brain ratios was killed just seven minutes after the alcohol was administered, the time interval being ridiculously short for medicolegal interpretation. Finally, their mathematical calculations are erroneous, since they inverted their dog brain-blood alcohol ratios when figuring possible brain alcohol variations in man. The importance of blood and spinal fluid alcohol has been adequately summed up by Bogen:

> Although Gettler's results, showing a closer relationship of brain alcohol to spinal fluid alcohol than to blood, seem contradicted by Newman and others, the differences between them would rarely lead to a change in diagnosis. On the other hand, there is available abundant data showing a close relation between blood alcohol and behavior.

It is true that chemical examination of the brain tissue would help solve the drunken driving problem by preventing individual repetitions of drunken driving and that spinal fluid alcohol is related to brain alcohol. But it is also true that the alcohol in the blood is responsible for the distribution of alcohol to the brain and all body fluids. Alcohol tends to disperse itself uniformly in the water of the body, so that, after equilibrium has been established, examination of any tissue or body fluid gives information regarding the unoxidized alcohol in the body. The urine, being a filtrate from the blood, is suitable for examination, although the alcohol readings are lower than those of the blood shortly after drinking. This low alcohol reading is to the advantage of the accused. A second specimen of urine taken about half an hour later will give a truer picture of his condition. That the urine is of great value in the practical confirmation of alcoholic influence was shown by Halporn when he was able to predict with remarkable accuracy the percentage of urinary alcohol from the examination of drivers who had been arrested for driving while under the influence of alcohol. Bogen has demonstrated that the alcohol of the spinal fluid and that of the urine are practically identical. This work was confirmed but not published by Heise, who also found in unpublished observations that the occasional discrepancies between blood and urine alcohols as described by Haggard were associated with close approximation of urine and spinal fluid alcohol levels. However, the amounts of alcohol in the urines under these unusual conditions have not been found to be high enough to have medicolegal significance. The value of tests for alcohol in the breath has been established by Harger, Haggard and Jetter. Although there is some disagreement regarding methods of analysis and interpretation of results, it is agreed that the expired air closely reflects the alcohol in the blood. Friedemann has shown that the alcohol in the saliva can be used to predict blood alcohol. That the blood alcohol furnishes an adequate criterion for medicolegal interpretation is generally accepted. The only disagreement comes from Gettler and his disciples. The apparent disagreements regarding the medicolegal interpretations of various levels of alcohol in body fluids arises from the misunderstanding between the expressions "under the influence" and "intoxication." Gettler, for example, finds that all individuals having more than 0.25 per cent alcohol in the brain are intoxicated but that there is a loss of sense of care or aggressiveness in persons who have between 0.10 and 0.25 per cent. Jetter reports "acute intoxication" in 100 per cent of persons having a blood alcohol above 0.45 but is nevertheless in complete agreement with the recommendation of the National Safety Council that a level of the blood above 0.15 per cent should be considered as definite evidence that a person is "under the influence." The National Safety Council's Committee on Tests for Intoxication and the Committee for the Study of Problems of Motor Vehicle Accidents of the American Medical Association have agreed that when the level of alcohol in the blood or its equivalent in other body fluids is below 0.05 per cent the influence by alcohol is doubtful; that most persons are under the influence when the alcohol percentage is between 0.05 and 0.15, but that the physical signs and symptoms should be carefully considered in rendering an opinion of "under the influence." All persons harboring 0.15 per cent or more of alcohol in their bloods are to be considered "under the influence," since they have lost, at least to some extent, some of that clearness of intellect and self control that they would otherwise possess. Laws embodying this interpretation have been passed by Indiana, Maine and New York, and the tests have been admitted as evidence in almost every state of the Union.

It is difficult to define stages of intoxication on the basis of alcohol percentages because of the differences in behavior of individuals. There is, however, a definite pattern, based on the fact that alcohol first of all affects that part of the nervous system which in its evolution was developed last and that, as the alcohol percentage rises, the more primitive parts of the nervous system are involved. When the higher centers are involved, which may occur with as little as 0.02 per cent alcohol in the blood, there is a sense of careless well-being or of bodily and mental comfort. The apparent stimulation arises from loss of inhibitions, associated with some loss of judgment and self-control, and particularly a blunting of the ability for self criticism. There is no obvious intoxication, and the individual in this state has probably not increased his chances for having an accident. A second stage begins with levels of alcohol somewhere between 0.05 and 0.15 per cent. The part of the nervous system which is now being affected extends to the centers concerned with the sensory and skilled motor functions. Hand-eye coordination becomes impaired, speech may be slurred and the individual may feel that he is detached from himself, so that he can observe with amusement or consternation the bodily actions

of his other self. The third stage begins at levels somewhere between 0.10 and 0.40 per cent, when the most primitive functions are disturbed. The intellectual processes of judgment and self criticism are virtually suspended, perception and coordination are impaired, and the individual can respond only to strong appeals to his emotions. However, even in this state he frequently pulls himself together sufficiently to impress onlookers with his sobriety, only to fall into a heavy sleep when the need for self control has apparently passed. Death usually occurs when the blood alcohol exceeds 0.40 per cent.

PREMENSTRUAL PAIN

To the Editor:—A married woman aged 41, without children, complains of severe pain in the lower part of the abdomen and the pelvis radiating to the back. The pain, which is described as being like a severe toothache, comes on each month about five days before menstruation is due. It strikes four or five times a day—more often during night than day—and lasts from five to ten minutes. The attacks are accompanied by the formation of a great deal of gas, but belching or passing gas from the bowel by using an enema does not stop the pain. These attacks have occurred every month for several years and always stop as soon as the menstrual flow starts. The patient had peritonitis in 1925 followed by the formation of an abscess in the abdomen, which was evacuated. Otherwise the history is not significant. The patient appears healthy and feels well except when these bouts of pain occur. Examination was essentially without significant findings except that the cervical canal seemed very narrow, but dilation a few days before the pains were due to start had no effect. All sorts of pain relievers, sedatives and hormone preparations have been tried without benefit.

H. W. Byrn, M.D., New Albany, Ind.

Answer.—This is indeed a puzzling case. The limitation of the symptoms to the few days before each menstrual flow may perhaps permit the association of this case with the syndrome known as premenstrual tension or premenstrual distress. The name premenstrual tension was given by Frank to a condition which is not uncommon. The symptoms start about a week before menstruation and may consist of headache, emotional instability, irritability and psychic depression. Frequently there occur abdominal distention, nausea and vomiting, increased sex desire, vulvar pruritus and sometimes edema of the vulva. Minor degrees of premenstrual distress are quite common but are accepted by many women without question as a normal feature of menstruation. When the disturbances become extreme, the condition is then assumed to be premenstrual tension. Frank has suggested that this condition is due to an increased concentration of estrogenic substance in the blood stream. Progesterone and testosterone propionate have been recommended as effective remedies. One to 5 mg. of progesterone or 5 to 10 mg. of androgen injected two or three times during the week preceding the anticipated menses has proved beneficial in some of these cases.

The hypothesis has been advanced by Greenhill and Freed (*Endocrinology* **26**:529 [March] 1940) that premenstrual tension is due to the increase in extracellular fluid of the various tissues such as the brain, gastrointestinal tract or skin. This edema gives rise to the symptoms which are typical of this condition. For this reason these investigators have treated their patients with ammonium chloride 0.6 Gm. three or four times daily, together with a sodium chloride free diet, starting at the midperiod and continuing to the beginning of menstruation in an attempt to cause a decrease in extracellular fluid. This therapy has benefited almost all patients who have been treated.

Some of the patients relieved had peculiar, localized edema. Perhaps in this case there is an undue amount of edema and distention of the intestine which produces the patient's symptoms. The attack of peritonitis may or may not be linked up with the patient's symptoms but probably not in view of the lapse of twenty years. Premenstrual intestinal distention is definitely relieved by ammonium chloride, and perhaps therefore the same treatment would help this patient.

DIAGNOSIS OF KERATOTIC LESION OF SKIN

To the Editor:—A man aged 60 has a cornified patch of skin about the size of a silver dollar on the back of his hand. This has been caused by too many x-ray treatments for an eczematous condition which he had on both hands for several years. What treatment is suggested?

M.D., Missouri.

Answer.—This lesion suggests at once the probability of a low grade squamous cell epithelioma. A biopsy should determine this point. If the lesion is merely hyperkeratotic, the application of an ointment containing 2 parts of 3 to 5 per cent salicylic acid in petrolatum and 1 part of lanolin should be of value. If the lesion has become neoplastic, vigorous fulguration should be used or excision with a skin graft if necessary.

SKIN TESTS IN ALLERGY

To the Editor:—Have there been any extensive studies of the correlation between skin tests with allergens and other allergic manifestations? Are there many instances of normal persons whose skin reaction is positive, although clinical manifestations of allergy to the substance showing the positive skin test are not experienced?

Perry B. Preston, M.D., Newark, N. J.

Answer.—In his presidential address, Dr. Louis Tuft presented to the American Society for the Study of Asthma and Allied Conditions a "Critical Evaluation of Skin Tests in Diagnosis." Much of the early work in this field was reviewed in the presentation.

Positive skin tests without any clinical sensitiveness to correspond are common enough. In 1935 Rackemann and Simon made skin tests by the intracutaneous method on 60 patients chosen at random in the medical wards and found that exactly half of them had positive reactions of varying size to some allergen. Since then, almost each day in a busy clinic, one can demonstrate patients with positive skin reactions who do not have symptoms to go with them. A common example is the patient who has hay fever in August with no trouble at all in June, and yet his skin tests made by the scratch method with pollen extracts in serial dilutions will show reactions to the grasses which may be even greater than the reactions to ragweed. In several cases in which treatment with pollen extract has been highly successful, the skin test made again after an interval of three years has been found still positive even though the patient has had no treatment and no symptoms in the meantime.

Such positive tests can be explained: "false positives" may depend on technic. As Sulzberger puts it, the skin is an "organ of memory." The positive tuberculin test can still be demonstrated in later adult life; and in a patient who in times past was clinically sensitive to a food or dust substance, the sensitiveness of the skin may be demonstrated in later years even though the sensitiveness of other organs has cleared away.

References:

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INTOLERANCE TO IRON MEDICATION

To the Editor:—A woman aged 29 breaks out with a skin rash whenever iron is given for a secondary anemia. The skin first has a macular eruption of the face, back and trunk, which later on becomes papular and painful. Usually about four or five lesions break out following the administration of iron. She states that, should she continue with the iron, these at times become pustular. I have used ferrous sulfate both with and without enteric coating, ferrous gluconate and calcium gluconate and lactate at the same time. Torantil has also been administered. Nothing seems to mitigate the development of this skin reaction.

M.D., Minnesota.

Answer.—An eruption of the skin is one of the common manifestations of intolerance to iron medication. In these patients it is necessary to depend on food iron after the cause of blood loss has been corrected. The diet should contain whole liver, well cooked meat, strawberries, peaches, apricots, molasses and other foods having easily available iron. If achlorhydria or hypochlorhydria is present, an adequate supplement of hydrochloric acid during the meal is advisable.

VITAL CAPACITY IN PREGNANCY

To the Editor:—Why is lung air capacity measured in pregnancy?

L. Edward Giovine, M.D., Woodside, N. Y.

Answer.—It is presumed that lung air capacity refers to vital capacity, which normally forms 72 per cent of the total lung volume. The vital capacity is decreased in patients with cardiac decompensation and other conditions in which the volume of the chest is decreased. It is not altered in patients with toxemia of pregnancy. The average vital capacity in normal women is 3,140 cc. ± 40 cc. Thomson and Cohen have followed the same patients throughout pregnancy and conclude that the vital capacity remains within normal limits in normal pregnancy, averaging 100 cc. increase at term and decreasing 138 cc. in the postpartum period. Plass and Oberst noted that the volume of tidal air and the minute volume of respired air increase progressively as term is approached and return to normal during the second week of the puerperium.

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